ANNALS OF SURGERY

VOL. 130 JULY, 1949 No. 1

CERVICAL ESOPHAGOGASTRIC ANASTOMOSIS FOLLOWING SUBTOTAL RESECTION OF THE ESOPHAGUS FOR CARCINOMA*

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IN 1942 Churchill and Sweet[1] reported the resection of the lower esophagus and used esophagogastric anastomosis for restoration of the continuity of the alimentary tract. In the same year, Wookey[2] demonstrated a technic for resection of the cervical esophagus. The entire intervening thoracic esophagus has now been shown to be accessible to treatment by surgical resection and esophagogastric anastomosis.

Garlock and Sweet demonstrated that the principle of esophagogastric anastomosis could be utilized for resection of tumors in the midthoracic esophagus by means of a supra-aortic anastomosis. More recently Garlock and Sweet have described technics for removal of the superior segment of the thoracic esophagus and have employed esophagogastric anastomosis in the cervical region.

Since the technic that we have used for resection of a carcinoma of the junction of the thoracic and cervical esophagus differs somewhat from those previously described, the following case is presented with a follow-up of nine months to demonstrate that this is a worth-while procedure from the point of view of palliation if not a cure.

CASE REPORT

C. D. (Bellevue Hospital No. 1731248), a 68-year-old unmarried magazine salesman, was admitted to Bellevue Hospital on April 6, 1948, with a chief complaint of regurgitating all fluids and food during the three previous days. The patient had had no complaints until two and one-half months before his admission, when he noted that solid food stuck in the upper part of his chest and he began to regurgitate his food two or three minutes after ingestion. There was no nausea and the food returned as taken, mixed with saliva. There was no blood in the regurgitated material. During two months prior to his admission the patient lived on a strictly self-imposed liquid diet. He finally came

* Given at the Joint Meeting of the Philadelphia Academy of Surgery and the New York Surgical Society, Wednesday, March 9, 1949. Submitted for publication, February, 1949.

into the hospital when for three days it had been impossible for him to swallow fluids without regurgitation. There had been no pain or cough. There was a 10-pound weight loss. The family history was significant in that a brother and sister had died of cancer. He had smoked six cigars a day for many years and drank moderately but regularly of beer and wine. The only serious illness he suffered in the past was jaundice 30 years previously. There was no history of venereal disease.

Physical examination revealed a thin, elderly man in no acute distress. The neck veins were distended and there was nodular enlargement of both lobes of the thyroid. The trachea was in the midline. There was no lymph-node enlargement. The chest was emphysematous with increased A.P. diameter. The lungs and heart were not remarkable.

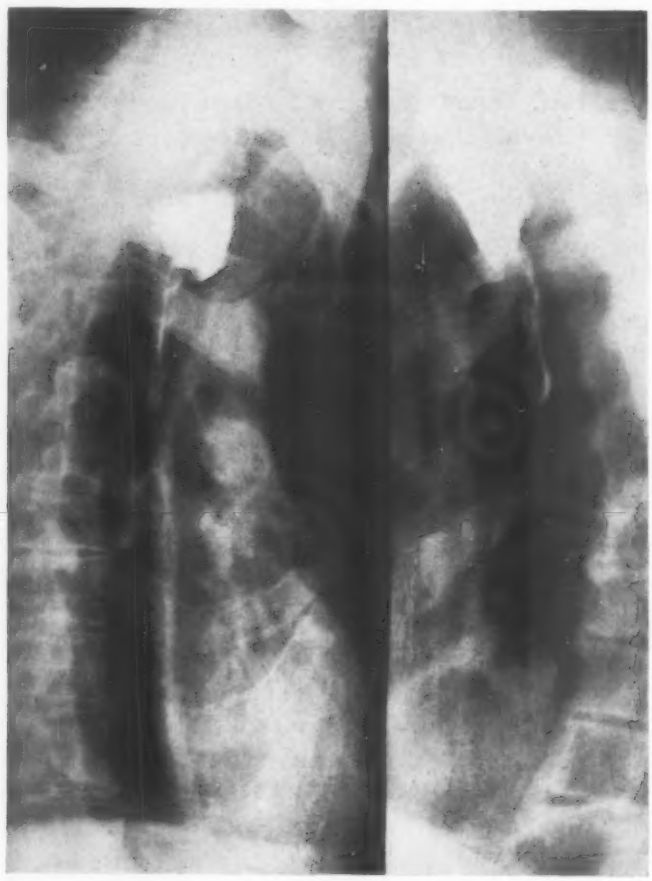

FIG. 1.—Complete obstruction of the esophagus due to carcinoma in the superior mediastinal segment.

The blood pressure was 110/78. The prostate was symmetric but twice the normal size. Fluoroscopic and roentgenologic examination after a swallow of barium showed a complete obstruction of the esophagus at the level of the first rib (Fig. 1). Esophagoscopic examination revealed a stenosing lesion of the upper esophagus, a biopsy of which was reported as a squamous-cell carcinoma. Bronchoscopy was negative.

The day after his admission, the patient was able to take fluids cautiously without regurgitation by the oral route. He was prepared for operation using a high protein

carbohydrate mixture with vitamins. Under the regimen he was able to gain back two pounds in the two weeks before operation.

Operation. On April 26, 1948, the operation was performed under intratracheal cyclopropane anesthesia in the right lateral recumbent position. A posterolateral incision was made over the course of the left seventh rib, curving upward at the lateral border of the paraspinal muscles. The seventh rib was removed subperiosteally from the cartilage anteriorly, to the transverse process posteriorly. A 1-cm. portion of the neck of the sixth rib was also excised to facilitate a more adequate opening of the chest. The parietal pleura was incised through the bed of the seventh rib and the thorax was widely opened with a rib spreader.

After exploration of the mediastinum for metastatic nodes, which were not encountered, an incision was made in the mediastinal pleura along the superior border of the arch of the aorta, curving upward posterior to the subclavian vessels to the dome of the thoracic cavity. Here the tumor of the esophagus could be felt as a hard, regular mass approximately 5 cm. in length extending upward into the base of the neck. At this point resection was decided upon. The mediastinal pleura was incised from below the arch of the aorta to the diaphragm. The esophagus was mobilized and dissected free from the mediastinum from the diaphragm to the arch of the aorta. The vessels from the aorta were secured by ligature and as much of the mediastinal lymphatic tissue as possible was removed with the esophagus. The arch of the aorta was mobilized at this point by ligature and division of the upper three intercostal arteries to facilitate the dissection of the esophagus in this region and to allow for future passage of the stomach through this area. After dissection of the esophagus from beneath the arch of the aorta, avoiding the recurrent laryngeal nerve, the dissection was then carried above, about the tumor and into the base of the neck. At this juncture the thoracic duct was encountered posteriorly in close proximity to the lower border of the tumor. It was doubly ligated and divided. The dissection was carried out well into the neck above the tumor, first by sharp dissection and then by finger until the operator's finger could be felt in the neck at the level of the cricoid cartilage.

With the completion of the dissection of the esophagus within the chest, the diaphragm was widely opened from the esophageal hiatus laterally in the direction of the muscular fibers. The phrenic nerve was not disturbed except as its branches were severed in incising the diaphragm. The greater curvature of the stomach was freed by incising the gastrolienal ligament, with ligature and division of the vasa brevia and the left gastro-epiploic vessels as far from the stomach as possible. The gastrocolic omentum was then completely incised to the pylorus, taking care to preserve the right gastro-epiploic vessel on the stomach. The stomach at this point was held up to allow dissection and ligation of the left gastric vessels at the coeliac axis. The gastrohepatic ligament was incised from diaphragm to pylorus well out from the lesser curvature of the stomach to preserve all anastomotic branches of the left gastric artery. In order to mobilize the duodenum more freely, incision of the peritoneum was made along its right lateral border. After thus freeing the stomach and duodenum, the stomach could be brought well up into the chest, and the pylorus could be brought up to the diaphragm without tension.

A small Payr clamp was placed across the cardiac orifice of the stomach, and the stomach was incised distally. Closure of the stomach was then carried out with an over-and-over continuous suture of chromic catgut as the stomach was cut. An inverting layer of interrupted 3-0 silk completed the closure of the stomach. The distal end of the esophagus was closed by purse-string suture, covered and tied securely within a rubber glove. A jejunostomy of the Witzel type was next performed at a distance of about 20 cm. from the ligament of Treitz, using a small catheter which was brought out through a stab wound made through the rectus muscle in the left upper quadrant. The esophagus was drawn above the arch of the aorta and preparation was made for incision in the neck.

The left arm was raised upward and suspended so as to allow access to the left neck. Incision was made along the anterior border of the sternocleidomastoid muscle, which

was retracted laterally. The left lobe of the thyroid was enlarged and nodular. A hemithyroidectomy was performed because it was felt that its size would definitely interfere with the intended anastomosis. By incising medial to the carotid sheath and inferiorly, the dissection plane of the esophagus was entered. The esophagus was drawn up into the neck wound and mobilized to the level of the thyroid cartilage. The stomach was then brought up beneath and to the right of the aorta and passed up into the neck through the aperture once occupied by the esophagus. The stomach thus lay in the normal position of the esophagus (Fig. 2). The apex of the stomach, which was a point on the greater curvature above the region of the gastrolienal ligament, was fixed by means of interrupted 4–0 silk to the prevertebral fascia of the cervical vertebrae. A row of interrupted mat-

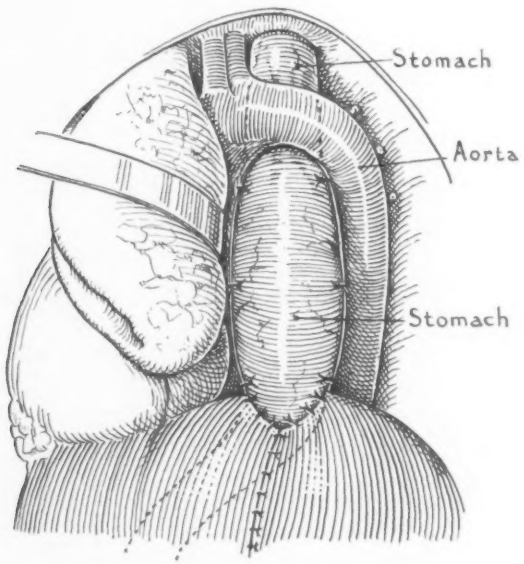

FIG. 2.—Diagram to show the position of the stomach in the thorax. The aorta has been mobilized by division of the upper three intercostal arteries.

tress sutures was placed between the anterior wall of the stomach and the posterior wall of the esophagus. A vertical incision was made in the stomach, 3 cm. in length. The esophagus was cut through, leaving the proximal cut surface for anastomosis. Through-and-through interrupted sutures of 4–0 silk were used to effect an anastomosis, these sutures going through all layers of both organs. Before closure of the anastomosis a Levin tube was passed through and drawn well down into the stomach. A supporting row of interrupted serosal sutures were placed anteriorly. The anterior surface of the stomach below the anastomosis was drawn cephalad and sutured above the anastomosis to the fascia on the thyroid cartilage and the under surface of the sternocleidomastoid muscle. The cervical wound was closed in layers about a small Penrose drain (Fig. 3). The stomach within the chest was fixed by interrupted sutures to the aperture at the base of the neck and to contiguous mediastinum down to the diaphragm, which was closed about the prepyloric area with interrupted silk. Through the eighth interspace in the axillary line a large fenestrated tube was introduced into the chest as a drain. The chest was closed in layers with interrupted silk sutures. The operative procedure consumed six and one-half hours, during which the patient received 2,000 cc. of blood and

1,000 cc. of 5 per cent glucose in saline for support. His condition throughout the procedure was satisfactory.

Pathologic examination of the resected esophagus was as follows: Macroscopic examination: The resected portion of esophagus measures 21 cm. in length. The proximal portion contains a firm, annular tumor, 4 cm. in length, which invades the wall of the esophagus and the adjacent connective tissue. The slitlike lumen measures 1 by 5 cm. and is not covered with mucosa. There is 1 cm. of grossly normal mucosa proximal to the lesion, but the tumor appears to extend to the line of surgical excision in the esophageal wall and the adjacent connective tissue.

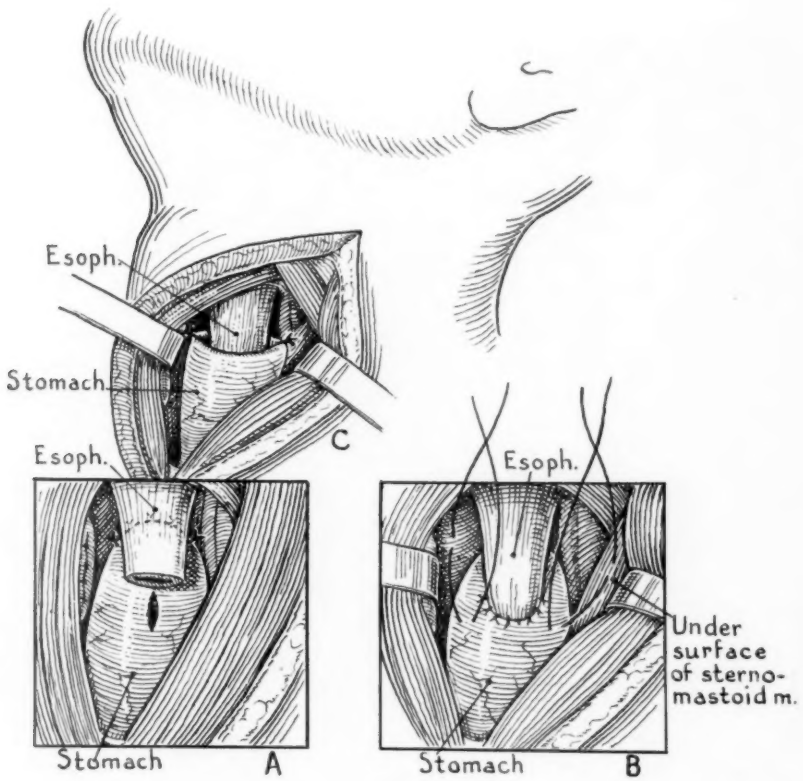

FIG. 3.—Schematic drawings of an esophagogastric anastomosis in the neck. (A) Fixation of the apex of the stomach to the prevertebral fascia and a row of sutures between the posterior wall of the esophagus and the stomach. (B) Supporting sutures placed following anastomosis. (C) Completed anastomosis.

Microscopic examination: Sections from the cardia show normal esophagus. Sections taken through the anterior wall of the esophagus, containing tumor, show normal stratified squamous epithelium, with the normal underlying wall from the distal portion of the esophagus merging into an area of ulcerated mucosa. The underlying wall in this area is invaded by stratified squamous epithelium growing in cords and sheets. Pearl formation is frequent. The proximal portion of the esophagus is covered with normal-appearing stratified squamous epithelium for a short distance. Sections of the thyroid reveal multiple adenomata.

Pathologic diagnosis: "Squamous-cell carcinoma of esophagus—adenomata of thyroid."

Postoperative Course. Between the second and the fourth days postoperatively, the patient had difficulty in raising bronchial secretions and developed several areas of atelectasis in the right lower lung field. This was controlled by means of vigorous and persistent tracheobronchial aspiration. The left lung remained well expanded and the chest tube drain was removed on the fourth day. Feedings were started through the jejunostomy catheter on the second postoperative day, and on the fifth, the nasogastric tube was removed. Fluid was then started cautiously by mouth. On the tenth day the patient was taking a six-feeding diet without difficulty and the jejunostomy tube was removed. At first, only small amounts of food could be eaten because of epigastric pain,

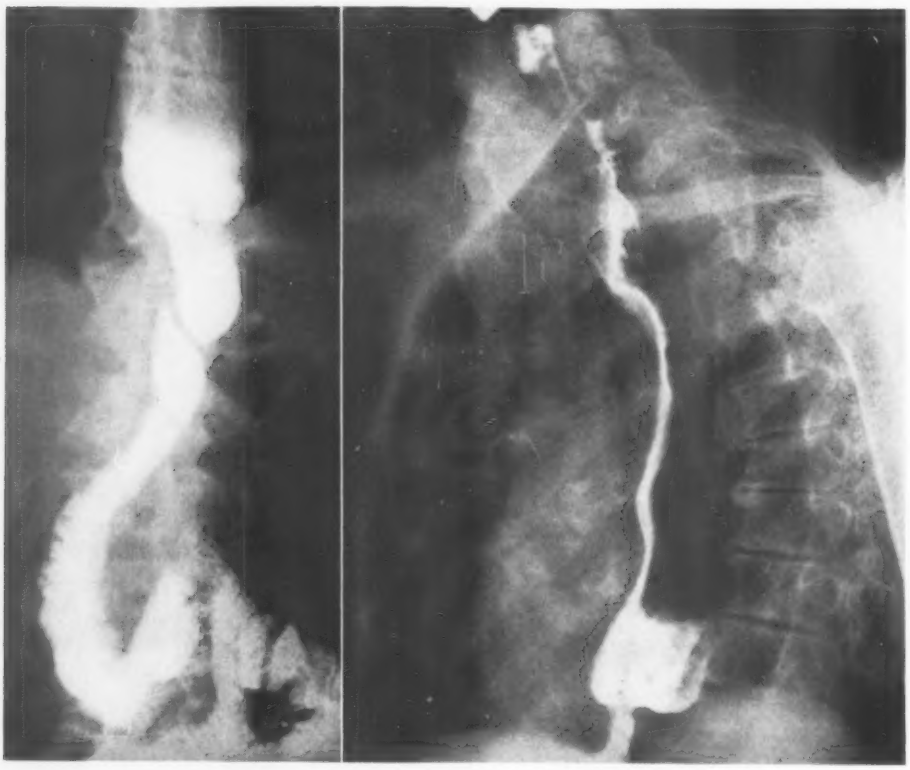

FIG. 4 FIG. 5

FIG. 4.—The pylorus is shown immediately below the diaphragm. Note the straightening of the duodenal curve.

FIG. 5.—A roentgenogram following a swallow of barium shows free flow through the esophagogastric anastomosis in the cervical region.

which ensued if the intake was too large. At the time of his discharge on June 10, 1948, the patient was beginning to gain weight and was eating without any discomfort. His stay in the hospital was prolonged by the complication of urinary retention, due to the benign hypertrophy of the prostate. Roentgen examination two days before discharge revealed evidence of esophagogastrostomy with the proximal fourth of the esophagus anastomosed to the stomach. No interference to the passage of barium through the site of anastomosis was noted (Figs. 4 and 5).

Follow-Up. One month after his discharge from the hospital and two and one-half months after the operation, the patient returned to his work as a magazine salesman, working from 9 to 5 daily except Sundays. When he was last seen, nine months after the operation, he weighed 142 pounds, having gained 36 pounds since his discharge from the hospital. His diet was not restricted and he had returned to his old habit of four glasses of beer a day and most of one bottle of Sherry wine on Saturday night. There has been no regurgitation of food, and the only discomfort he feels is epigastric pain on the rare occasion when he eats too large a meal.

DISCUSSION

In carcinoma of the junction of the supra-aortic thoracic esophagus and the cervical esophagus in which there is no demonstrable evidence of spread of the tumor as evidenced by palpable cervical lymph nodes, involvement of the recurrent laryngeal nerve or encroachment on the trachea by bronchoscopic examination, we believe exploratory thoracotomy is justified to determine operability. Experience may demonstrate, however, that even in those cases that fulfill the above criteria, an initial exploration of the neck may be practical in determining operability.

The decision to use the technic of resection and anastomosis described above was made during the course of the operation, as this method offered the most direct approach to the problem. The mobilization of the stomach through the thorax in the normal position occupied by the esophagus seemed a more direct and natural position for the gastric esophagus than to the left of the aorta, where the route to the neck aperture was more circuitous. The maneuver that was employed in this case of handing up the stomach through the neck by one operator in the chest wound to the other operator in the neck is not entirely satisfactory, but it was felt to be less traumatic to the stomach than using some method of suture to the esophagus for pull through after closure of the chest. It had been planned to remove the medial portion of the clavicle and part of the first rib to give a better exposure for the anastomosis, but in this particular case this procedure did not seem necessary, possibly because the large left lobe of the thyroid had created a greater space than usual in this area of the neck.

The performance of a jejunostomy at the time of operation is probably superfluous when it has been unnecessary as a preoperative means of establishing better nutrition. However, it did provide a good means of keeping up nutrition postoperatively during the six days before it was deemed wise to allow food by mouth.

SUMMARY

A case of carcinoma of the junction of the thoracic and cervical esophagus is presented with resection and esophagogastric anastomosis in the left cervical region. Follow-up of nine months is available on this patient to demonstrate the value of this procedure for palliation, if not for cure.

Note: This patient is alive and well 14 months after operation.

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ONE-STAGE RESECTION OF CARCINOMA OF THE CERVICAL ESOPHAGUS* WITH SUBPHARYNGEAL ESOPHAGOGASTROSTOMY

REPORT OF A SUCCESSFUL CASE

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INTRODUCTION

SURGICAL EXTIRPATION of carcinoma of the cervical esophagus presents a complex technical problem because of the difficulty in providing a suitable replacement for the resected esophagus when extensive excision is necessary. In 1946, in the course of an operation to remove a supra-aortic carcinoma of the esophagus, the author performed a complete mobilization of the stomach to provide an adequate esophageal substitute. When the esophagogastric anastomosis was made just under the dome of the pleural cavity, an excess of from four to five inches of the gastric tube was available. At that time it was realized that it was technically feasible to bring the stomach into the neck for an esophagogastric anastomosis. Since then, we have explored a small number of cases of carcinoma of the cervical esophagus with the intention of replacing the resected cervical esophagus with the stomach. It was not until September 10, 1948, that an operable case was found. This communication consists of an account of surgical problems encountered in a successful one-stage resection of carcinoma of the cervical esophagus and a subpharyngeal esophagogastrostomy.

Since 1884, various types of skin tubes have been fashioned to replace the resected cervical esophagus.[1-4] When the tumor extends into the thoracic cavity, it is impossible to employ the simple types of skin tubes. The year 1948 has seen a renewed interest in the treatment of carcinoma of the cervical esophagus. Bricker and Burford[5] devised a multi-stage method of transplanting a pedicled, skin-lined tube into the thorax to replace the thoracic, as well as the cervical, portion of the resected esophagus. Following the first successful resection of carcinoma of the thoracic esophagus with esophagogastrostomy in this country by Adams and Phemister,[6] the soundness of the technic of bringing the stomach up into the chest to replace the resected esophagus has been well proved. Sweet[7] and Garlock[8] have reported this year the performance of a cervical esophagogastric anastomosis in cases of high intrathoracic carcinoma of the esophagus. Sweet resected the first rib and clavicle with a successful result in two cases. Garlock did not resect the clavicle or rib, but lost his patient on the day after operation. In 1948, O'Donnell,[9] also, performed a resection of carcinoma of the cervical esophagus with a simultaneous cervical esophagogastrostomy. The cricopharyngeus muscle was severed, with

* Submitted for publication, January, 1949.

resultant regurgitation of gastric juice and subsequent pharyngeal ulcers. As far as we know, O'Donnell's and the author's patients represent the only two reported cases of resection of the cervical esophagus, with one-stage esophagogastrostomy.

CASE HISTORY

W. C., a 59-year-old carpenter, was admitted to the hospital on September 6, 1948, complaining of dysphagia of six weeks' duration. Food was regurgitated immediately after swallowing and he felt an obstruction in his throat. He was able to swallow only liquids, a sip at a time. For 14 months, he had been confined to his home because of a polyarthritis involving the large joints and had lost 50 pounds in weight. There had been an additional weight loss of 15 pounds during the six weeks before his admission. Previously he had been well except that a shell explosion had fractured his right wrist and jaw in World War I.

FIG. 1.—Preoperative upper gastro-intestinal series. Irregular obstruction to the flow of barium in the cervical esophagus is seen approximately one and one-half inches above the clavicle. The findings are typical of carcinoma of the cervical esophagus.

On examination, a very emaciated, elderly white male was seen who appeared to be chronically ill. The skin was loose and dry. Other positive findings included a barrel-shaped chest with limited expansion. Fine râles were heard at both bases. The heart

was normal and the abdomen was markedly scaphoid, with the liver edge felt 3 cm. below the costal margin. Limitation of motion and swelling of the large joints of the arms and legs were present. No enlarged peripheral nodes were felt.

Roentgen barium study of the esophagus showed an irregular filling defect above the clavicle, typical of carcinoma (Fig. 1). On esophagoscopy, a friable tumor was found 2.5 cm. below the cricopharyngeus. Biopsy revealed squamous-cell carcinoma, grade III. No gross involvement of the trachea was found on bronchoscopy. Laboratory studies showed hemoglobin, 87 per cent; red blood count, 4,490,000; white blood count, 9,500; polymorphonuclears, 56 per cent; lymphocytes, 36 per cent; mononuclears, 2 per cent; and eosinophiles, 6 per cent. The N.P.N. was 25 mg. per cent; serum albumin, 4 per cent; and serum globulin, 2.7 per cent. The urine showed a trace of albumin and rare leukocyte on stained smear. The patient was placed on a 200 Gm. protein, high-vitamin,

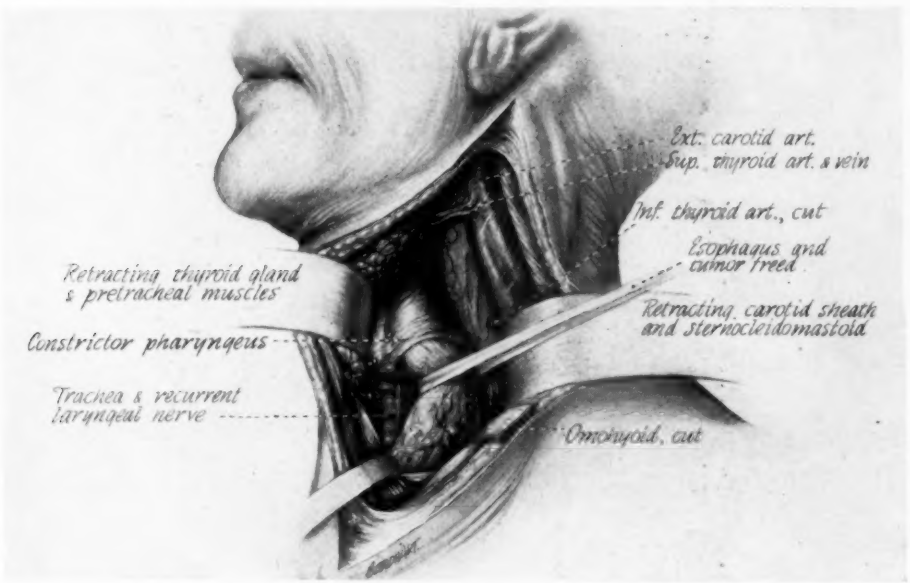
Ext. carotid art.
Sup. thyroid art. & vein
Inf. thyroid art., cut
Esophagus and tumor freed
Retracting thyroid gland & pretracheal muscles
Retracting carotid sheath and sternocleidomastoid
Constrictor pharyngeus
Trachea & recurrent laryngeal nerve
Omohyoid, cut

FIG. 2.—The cervical esophagus has been exposed and freed from the trachea through an incision anterior to the sternocleidomastoid muscle.

3,000-calorie, low-sodium, liquid diet. Three hundred thousand units of penicillin, 1.0 Gm. of streptomycin, 1,000 mg. of vitamin C, and vitamin B complex were administered intramuscularly daily.

OPERATIVE REPORT

On September 10, 1948, the operation was performed. After a pentothal induction, endotracheal ether-oxygen was used for maintenance. A blood transfusion was started at the beginning of the operation and continued throughout, 2,000 cc. being given. The patient was placed on his right side and the left thoracic and cervical regions were prepared for operation. A sterile stockinette covered the left arm, so that it could be moved to give greater exposure of the neck and chest (Fig. 3A). An incision was made in the neck, extending from the angle of the jaw on the left down to the suprasternal notch. After severing the platysma, the sternocleidomastoid muscle was retracted laterally. The inferior thyroid vessels were ligated and the carotid sheath retracted laterally. Dissecting behind the thyroid gland, the trachea and the thyroid cartilage were identified

and the esophagus was found to be infiltrated with a hard, firm mass, obviously carcinoma. By careful dissection, it was possible to free the esophagus from the trachea (Fig. 2). Although cancerous tissue was in apposition to the posterior tracheal wall, there was no gross involvement of the trachea. The cancerous tissue extended down into the superior mediastinum. A Penrose sheath drain was placed about the esophagus, which was involved with tumor tissue to approximately 2.5 cm. from the cricothyroid pinch cock.

The chest cavity was opened through an S-shaped incision, centering over the sixth rib (Fig. 3A). After severing the muscles of the back, the sixth rib was removed and the fifth and seventh ribs sectioned posteriorly and the seventh anteriorly. An excellent

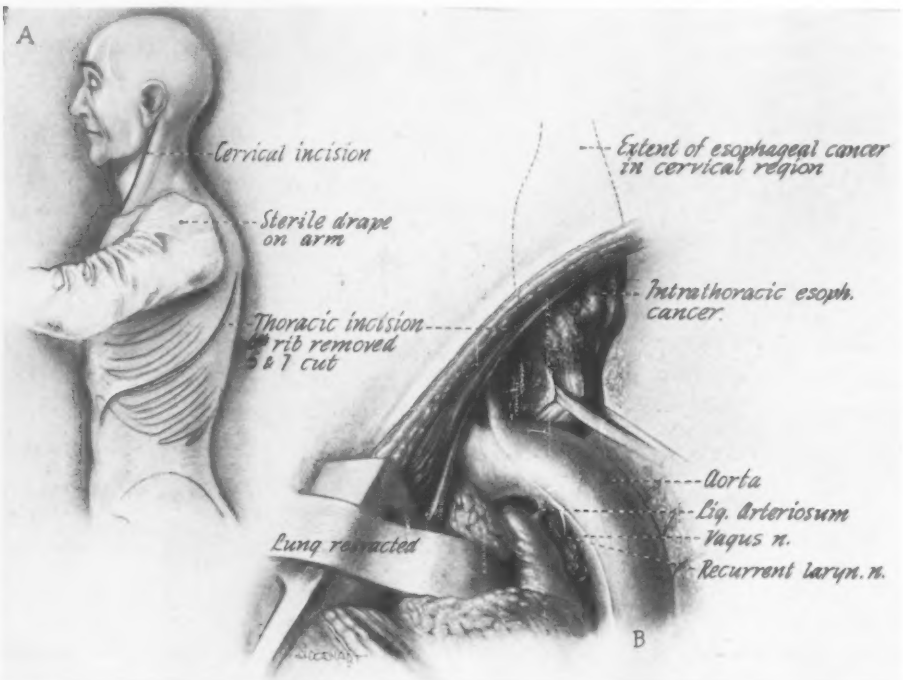

FIG. 3.—A. Cervical and thoracic incisions are used. The patient is lying on his right side. The left arm is covered with a sterile drape. Mobility of the arm facilitates exposure of neck and thorax.

B. Freeing of the thoracic esophagus above the aortic arch through the thoracic approach.

view of the entire pleural cavity was obtained. Dissecting into the superior mediastinum, the cancerous tissue seemed to be limited to the esophagus, so that resection was decided upon (Fig. 3B).

The diaphragm was incised, starting at the hiatus and extending around to the sternal junction, making a curved incision.[10] The stomach was exposed and the mobilization of the stomach was begun by severing the vasa brevia. The left gastroepiploic vessels were saved to preserve the blood supply to the stomach. Reflecting the stomach forward, the coronary vessels were dissected out and ligated, exposing the left gastric artery and vein. The smaller divisions of these vessels were sutured individually to prevent puckering of the lesser curvature of the stomach. Further freeing of the stomach was performed, down to the duodenum, where adhesions binding the pylorus and the first part of the duodenum to the posterior abdominal wall were released to give the

maximum mobility to the stomach. The thoracic esophagus was exposed by opening the inferior pulmonary ligament, retracting the left lung mesially. The inferior phrenic vessels and the segmental vessels from the aorta were ligated. The esophagus was then mobilized behind the arch of the aorta, taking care not to enter the right pleural cavity. The esophagus was doubly clamped at the cardia with Payr clamps and divided. The cut end of the esophagus was covered with a Penrose drain, which was ligated to prevent leakage of the esophageal contents. The distal end of the esophagus was then turned into the cardia of the stomach and closed with two running layers of No. 0 chromic, reinforced with interrupted sutures of fine silk. The esophagus was then liberated to the point where the cervical esophagus had been mobilized. This was done by ligating the

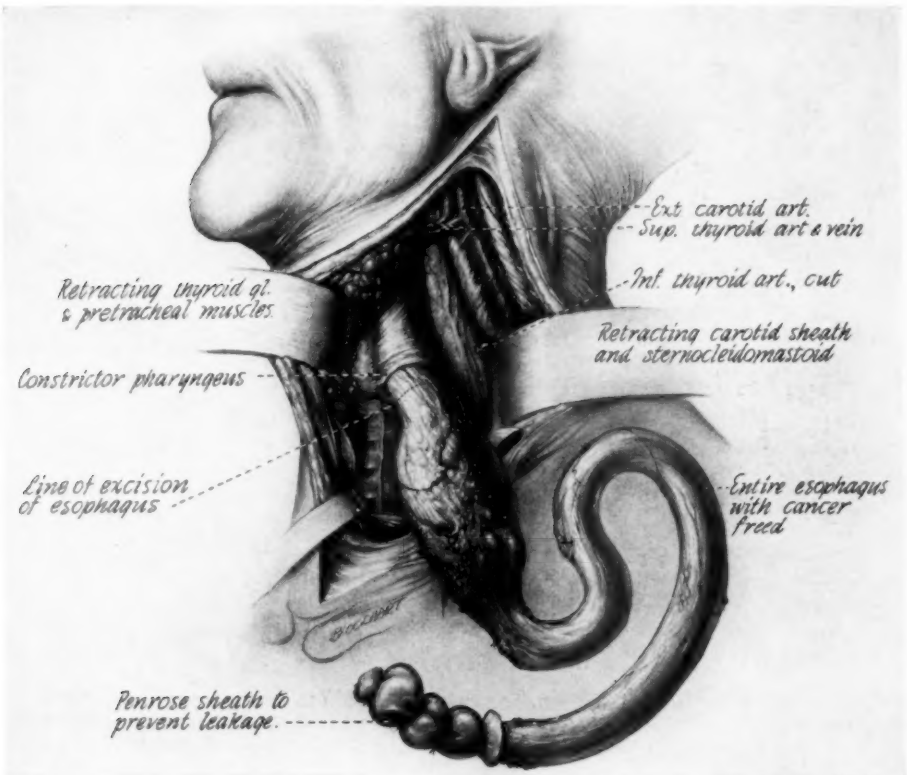
Ext. carotid art.
Sup. thyroid art. & vein
Inf. thyroid art., cut
Retracting thyroid gl. & pretracheal muscles
Retracting carotid sheath and sternocleidomastoid
Constrictor pharyngeus
Line of excision of esophagus
Entire esophagus with cancer freed
Penrose sheath to prevent leakage.

FIG. 4.—The entire thoracic esophagus has been drawn up into the cervical wound.

esophageal branches of the inferior thyroid artery. The esophagus was then pulled out through the reopened cervical incision, which had been lightly closed with a few mattress sutures. Keeping the left gastro-epiploic vessels on the left side and the lesser curvature on the right, the stomach was moved into the thorax. It was brought up *behind* the arch of the aorta in the normal esophageal bed and thence to the dome of the pleural cavity and up into the neck.

The operation was then continued in the cervical region, and the entire thoracic esophagus pulled up into the cervical wound (Fig. 4). We were pleased to find that it was possible to bring the stomach up to the level of the cricothyroid pinch cock. Two small pieces of omentum had been saved to reinforce the anastomosis. A circular incision 2 cm. in diameter was made in the fundus of the stomach, which was just below the

most cephalad portion of the stomach, and several bleeding vessels were ligated. The stomach had a slightly bluish appearance, and was not as pink as we are accustomed to see it for an intrathoracic esophagogastric anastomosis. This apical portion of the stomach was sutured to the esophagus just below its junction with the pharynx at the cricothyroid pinch cock. We wished to preserve the pinch cock to prevent regurgitation of gastric contents into the mouth. The anastomosis was then made with interrupted No. 0000 silk, first uniting the posterior muscularis of the esophagus to the serosa of the stomach. The esophagus was then amputated and a careful circumferential layer of sutures was placed to unite the esophageal and gastric mucosae together (Fig. 5A). Anteriorly the muscularis of the esophagus and the serosa of the stomach were then

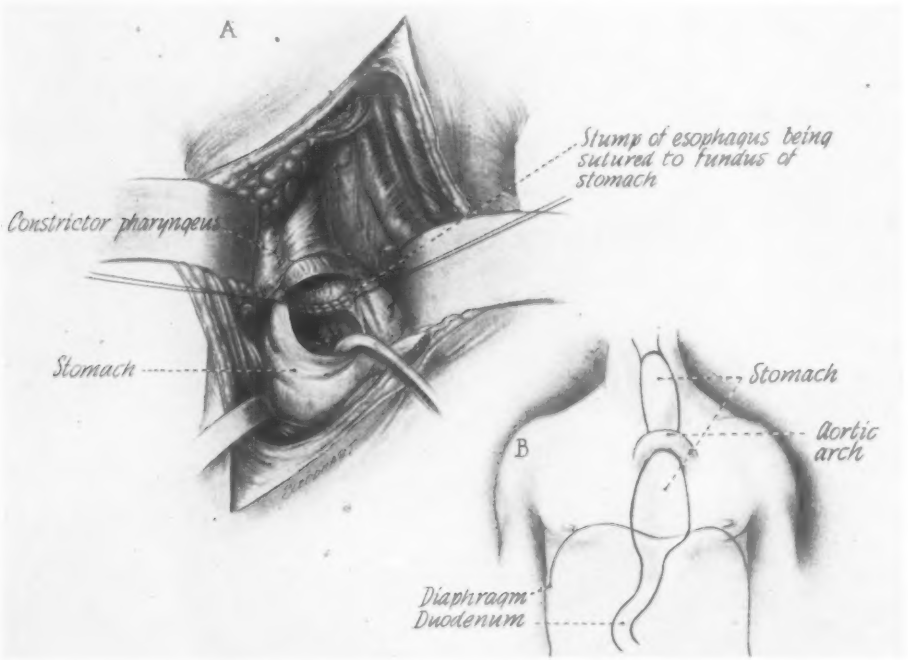

FIG. 5.—A. A careful three-layer open anastomosis of the stomach and esophagus is made with No. 0000 silk.
B. The position of the stomach in the thoracico-cervical region is shown diagrammatically.

approximated. A few interrupted sutures were taken to make a third layer of closure, muscularis to serosa; and the omentum which had been saved was further tacked to the anastomosis to reinforce it. The stomach was then fixed to the cervical tissues with interrupted sutures of fine silk. Penrose drains were inserted inferiorly toward the superior mediastinum and superiorly to the region of the anastomosis. The wound was closed in layers with interrupted fine silk, bringing together first the ribbon muscles of the neck, then the platysma and the skin. The thorax was entered, and the stomach was sutured to the superior mediastinal pleura with interrupted silk sutures to seal off the thorax from the cervical region. In fixing the stomach to the adventitia of the descending aorta, one suture struck a branch of the left gastro-epiploic artery and a hematoma, 2 cm. in diameter, developed in the gastrocolic omentum. The bleeding stopped spontaneously. The diaphragm was closed with interrupted silk sutures, imbricating with running No. 1 chromic catgut. The stomach fell posteriorly in the esophageal hiatus and was attached

anteriorly to the diaphragm with fine silk sutures. Drainage tubes were left in the second and eighth intercostal spaces and connected to a closed water-seal drainage system. The wound was washed out with saline. Because of the wide opening of the rib spreaders, the costal cartilage at the sixth and seventh chondral junction had been fractured, so that it was necessary to repair this fracture with two sutures of heavy silk. Closure was effected using No. 1 chromic catgut for the deep muscles, No. 000 chromic for the superficial fascia and silk for the skin. Despite the long, tedious operation (nine and a half hours), the patient was not in shock at the end of the surgery. The blood pressure was 100/60, pulse 100 and respirations 22. Figure 5 shows diagrammatically the position of the stomach at the end of the operation.

The report of the pathologic specimen is as follows: "The gross specimen consists of a resected segment of esophagus which measures 22.5 cm. in length. Near one extremity of the specimen the lumen is almost completely occluded by an annular carcinomatous tumor mass which measures 55 mm. in length. Section through this shows cellular, grayish-pink tumor tissue infiltrating through the thickness of the esophageal wall. The mucosal surface above this point is intact and pinkish gray in color.

Histologic examination of sections taken through the tumor mass described above shows that it is made up of irregular clusters and strands of epithelial cells of squamous type. These form occasional epithelial pearls. There are frequent mitotic figures and hyperchromatic nuclei. Tumor cells are seen within the lumina of small vascular spaces in the muscularis. The diagnosis is squamous-cell carcinoma, Grade III, of esophagus." Angus Wright, M.D., Pathologist.

POSTOPERATIVE COURSE

Oxygen was given per nasal catheter with CO_2 inhalation every half hour till the patient was awake and then every 2 hours. The patient was turned from one side to the other at two-hour intervals. Demerol in 50 mg. doses was used for pain and he was placed in Fowler's position as soon as he was awake and could cough. Penicillin, 50,000 units, every 3 hours, and streptomycin, 1.0 Gm. daily, were administered, intramuscularly. A Levine tube was placed in the stomach and connected to a Chaffin-Pratt suction machine for 24 hours to prevent regurgitation of stomach contents into the pharynx. The anterior thoracic intrapleural drainage tube was clamped 4 hours after operation and 100,000 units of penicillin in 30 cc. normal saline were injected into the pleural cavity. The clamp was released after 6 hours.

The temperature was 102° (rectal); pulse, 120; and respirations, 28 on the first postoperative day. The left lung was expanded and signs of patchy atelectasis in the right lower lobe were present on the second postoperative day. By means of a rubber catheter, passed without anesthesia transnasally into the right main bronchus, 10 cc. of thick gluelike mucus were aspirated. This procedure was repeated 5 times during the next two days until the right lung was entirely clear. The temperature fell to 100° (rectal); pulse, 90; respirations, 22 on the third postoperative day; the drainage tubes were removed from the left chest and the patient was allowed out of bed. Intravenous fluids consisting of 2,000 cc. of 5 per cent glucose in water and 1,000 cc. of 5 per cent glucose in saline were given daily. On the fourth postoperative day, fluids were started by mouth, one ounce of water every hour. Swallowing was difficult at first as there was bulging of the left side of the neck, apparently from dilatation of the stomach. The patient coughed with this dilatation, which was interpreted as evidence of pressure on the trachea. The wounds healed per primam and the drains were removed from the neck on the eleventh postoperative day.

Roentgen studies were made 15 days after the operation. Figure 6 shows barium outlining the stomach, which has a retrocardiac position in the thorax and is located in the neck in the esophageal bed. The lung fields are otherwise normal. Figure 7A demonstrates a detail of the gastric outline in the upper thorax, as shown by the introduction

of barium. The aortic arch constricts the posterior-lying stomach, and partly acts as a cardia. Figure 7B illustrates the straightening out of the duodenum beneath the stomach, which is almost entirely intrathoracic in position. The satisfactory emptying of the duodenum into the jejunum is seen in Figure 8.

The coughing, associated with eating, gradually subsided and the patient was discharged on the sixteenth postoperative day on soft diet, 2,570 calories with proteins, 140; carbohydrates, 199; and fats, 123. He continued to gain in weight (10 pounds) and strength. The swallowing improved so that there was only an occasional coughing following the ingestion of food. Esophagoscopy three months after the operation showed a slight stricture of the anastomosis at the level of the cricopharyngeus, which admitted a No. 30 French dilator readily.

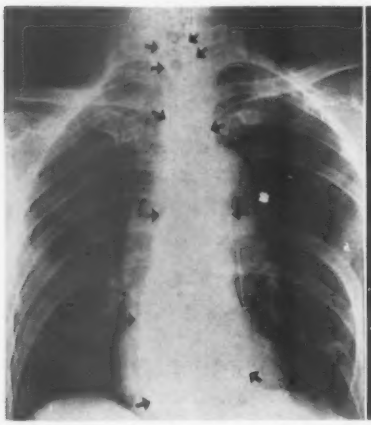

FIG. 6

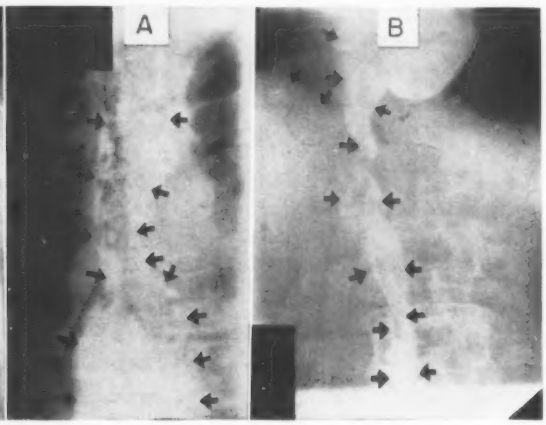

FIG. 7

FIG. 6.—Upper gastro-intestinal series taken 15 days after operation. The stomach lies behind the heart in the thorax and extends up into the neck in the esophageal bed. The lung fields are clear. The sixth rib has been resected.

FIG. 7.—(A, *left*) Detailed barium study of the stomach in the upper thorax demonstrates the constricting effect of the aortic arch on the stomach.

(B, *right*) The pylorus of the stomach is near the diaphragm and the duodenum is straightened out.

DISCUSSION

The success of this operation is dependent upon attention to many details which we have emphasized for the surgical resection of carcinoma of the upper third of the thoracic segment of the esophagus.[10] In addition, certain other points should be mentioned. The extensive mobilization of the stomach, necessary to bring it up into the neck, is effected by freeing the entire stomach, pylorus and duodenum. Greater care must be observed in preserving the blood supply to the stomach and duodenum than for an intrathoracic mobilization of the stomach. This can be done by: (1) preserving a generous cuff of omentum along the greater curvature; (2) freeing the pylorus and the duodenum by blunt dissection; (3) avoiding tension and torsion on the stomach. To mobilize the duodenum, one may excise the peritoneum lateral to the duodenum, as advocated by Priestley and Kumpuris[11] for the performance of an esophagoduodenal anastomosis in total gastrectomy. The

ligation of the individual branches of the left gastric artery and vein permits more stretch to the lesser curvature so that the stomach is a straight tube, rather than a comma-shaped curved organ. Greater length of the gastric tube can be obtained by placing it behind the arch of the aorta in the esophageal bed. This will give an additional 2 to 4 cm. of length to the stomach. Besides this, the aortic arch will constrict the posterior-lying stomach and tend to prevent the regurgitation of fluid cephalad to the aortic arch when the patient is lying down (Fig. 7A).

FIG. 8.—The barium is seen to enter the jejunum freely from the straightened-out duodenum.

After making the cervical anastomosis, the omentum, brought up into the neck, will help reinforce this union. A closure of the mediastinal pleura about the stomach at the thoracic inlet will tend to isolate the cervical regions from the thorax. If a breakdown in the anastomosis occurs, then the drainage will escape through the cervical tissues, along the track made by the cervically placed Penrose sheath drains. Even though the drainage in our case was nil,

we left these drains in 11 days to form a definite track for escape of infected fluid from a possible leak in the anastomosis. The anastomosis in our case healed per primam.

It is advisable to preserve the cricopharyngeus muscle, if possible, in order to prevent regurgitation of gastric juice into the pharynx and thus avoid pharyngeal and oral ulcerations. With this muscle intact, no regurgitation of gastric juice was experienced in our case. As mentioned before, the placing of the stomach behind the arch of the aorta probably also tended to lessen the regurgitation. The cough following the ingestion of food, soon after operation, may have been due to: (1) pressure of the stomach on the trachea; (2) cricopharyngeal spasm, or distortion of this muscle, possibly traumatized by suture, or (3) actual stenosis at the esophagogastric junction. The fact that this symptom, which was troublesome soon after operation, gradually improved makes us believe that it was mainly due to the first two causes. It is true that there was some stenosis at the anastomosis (No. 30 French), yet we have observed patients with stenosis much smaller than this who could swallow fluids and soft solids without regurgitation and cough.

The question occurs, will it be possible always to mobilize the stomach sufficiently to bring it up into the neck for anastomosis? This question cannot be answered at the present time. The stomach in the present case was of average size. It is true that great difficulty might be encountered in obtaining sufficient mobilization of a greatly contracted stomach. The gastro-intestinal series may throw some light on this problem. With the use of very thin barium, it may be possible to outline the size of the stomach. Gastric barium studies in our case indicated a normal-sized stomach. A greatly contracted gastric shadow would probably contraindicate this procedure. It is wise not to injure the blood supply to the esophagus until the diaphragm has been opened and the size of the stomach determined accurately. If it was proved impossible to mobilize the stomach well into the neck, a high thoracic gastrostomy could be performed and the defect bridged by a skin tube. The anticipated result of such a procedure would be less desirable than could be expected for the one-stage operation presented here.

In addition to careful preoperative preparation of the patient, meticulous surgical technic and skillful anesthesia, so administered as to prevent hypoxia and shock, the postoperative care is extremely important.[10] The routine use of penicillin and streptomycin have made mediastinal and intrapleural infection less of a problem for the resection of carcinoma of the esophagus, regardless of the location. Besides the maintenance of nutrition and fluid and salt balance during the early postoperative period, the prevention and management of postoperative pulmonary complications is of prime importance. The success of the operation often hinges on this one factor. In our case, despite diligent precautions, a patchy atelectasis of the right lower lobe developed. We employed catheter aspiration of the trachea and bronchi[12, 13] six different times during the second and third postoperative days. Certainly without this

meticulous attention to the bronchial toilet, all our previous hard work on this case would have been in vain.

The operation of Bricker and Burford fulfills the requirement of resection of extensive carcinoma of the cervical esophagus in which the upper thoracic esophagus is also involved. Actually they performed a bilateral neck dissection at the first stage, so that a more thorough removal of carcinoma in the lymphatic channels was effected. Their operation has the inherent disadvantage of all multi-stage operations for cancer in which a considerable period of time is required for the completion of the plastic procedures. The carcinoma may recur soon after the skin tube is completed. In the time necessary to fashion the tube, the patient has been unable to swallow and has been fed by a gastrostomy. The one-stage operation we have presented is superior from this point of view in that the patient can swallow soon after the operation has been completed. Thus, even if recurrence of the carcinoma develops, successful palliation has been promptly effected. The disadvantage of the one-stage operation lies in the fact that a bilateral neck dissection was not performed. This might be done as a preliminary operation, at which time the operability of the carcinoma could be determined. Whenever the carcinoma cells extend from the esophageal mucosa through the muscularis and are in approximation with, or invading, the adjacent structures (a common finding in these cases), permanent cure cannot be expected and only palliation is effected. In our case the carcinoma cells had extended through the esophageal muscularis, so that recurrence may be anticipated. A great deal more experience will be necessary for the true evaluation of the multi-stage and the single-stage procedures.

SUMMARY

1. A case of successful one-stage resection of carcinoma of the cervical esophagus with a subpharyngeal esophagogastrostomy has been presented.

2. The surgical problems involved in the resection of carcinoma of the cervical esophagus and the cervical esophagogastric anastomosis have been discussed.

3. This operation offers hope for one-stage resection of the tumor and immediate return of swallowing to these miserable patients with carcinoma of the cervical esophagus in which there is extensive involvement in the cervical region or an extension of the cancer into the thoracic esophagus.

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CERVICAL ESOPHAGOGASTROSTOMY FOLLOWING RESECTION OF SUPRA-AORTIC CARCINOMA OF THE ESOPHAGUS*

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IN THE PAST FEW YEARS partial esophagectomy plus primary intrathoracic esophagogastrostomy has become the operation of choice for removal of carcinomas of the lower two-thirds of the thoracic esophagus. Until recently, however, this technic seemed unsuitable for cancers located in the upper third, that is in the supra-aortic part of the thoracic esophagus.

A few months ago Garlock[1] described a combined cervico-thoracic approach which permits excision of the entire thoracic esophagus and restoration of the alimentary canal by means of a cervical esophagogastrostomy. Garlock's patient died on the morning of the first postoperative day of what Garlock believes were "profound physiological disturbances possibly caused by vagal stimulation." Garlock's technique was employed in the case to be reported, and the description will be given in the operative report.

CASE REPORT

A 61-year-old white male was admitted to the Jewish Hospital of Brooklyn on December 10, 1948, because of difficulty in swallowing for the preceding six weeks. This began as a feeling of heaviness while swallowing and progressed rapidly so that at the time of admission he could not swallow solid food. He could take liquids in small amounts. Solid food or large swallows of liquids seemed to become blocked in the region of the jugular notch and were regurgitated. There was a 7 lb. weight loss, but no cough, fever, pain nor change in speech, and with no melena or hemoptysis.

Past History. In 1937 amputation of the penis and bilateral inguinal node dissection was performed for carcinoma of the penis. He has had no subsequent difficulty in voiding and no evidence of recurrence. There has been a partial bilateral difficulty in hearing for the past three years.

Physical Examination. T. 99 B.P. 124/64. Pulse 68. Resp. 20. The patient is a well developed, thin white male. There is no evidence of recent weight loss. The penis has been amputated at its base, the meatus is patent and he voids in a good stream. There are bilateral 6-inch inguinal scars. Remainder of physical examination is negative except for partial deafness. Impression at time of admission: carcinoma of the esophagus. The patient was esophagoscoped and a biopsy taken from a tumor mass in the upper esophagus.

Pathologic Report: Tissue from esophagus showed evidence of epidermoid carcinoma.

Roentgen-ray examination of the esophagus by means of a barium swallow revealed a narrowing between the level of the jugular notch and the upper border of the aortic arch. Only a trickle of barium was seen to pass through the constricted area (Fig. 1).

Laboratory Data on Admission: Blood count: Hgb 88 per cent, RBC 4.35, WBC 7000, 38 per cent polys, 61 lymphs, 1 eosin. Urine: acid, 1.020, trace of albumin. O sugar.

Blood chemical determinations: sugar 85 mg. per 100 cc.; urea 9 mg. per 100 cc., CO_2 69 vol. per cent, chloride 354 mg. per cent, prothrombin time normal, phosphorus 3.4 mg. per cent, alkaline phosphate 2.2 Bodansky units per cent, total protein 6.2 per

* Submitted for publication, March, 1949.

cent, albumin 3.6 per cent, globulin 2.6 per cent, Mazzini negative. Electrocardiogram was normal.

The patient was prepared with blood transfusions and hydrated with intravenous glucose and saline solutions and the operation performed on December 17, 1948, under endotracheal cyclopropane, ether, oxygen anesthesia. He was placed on the table slightly

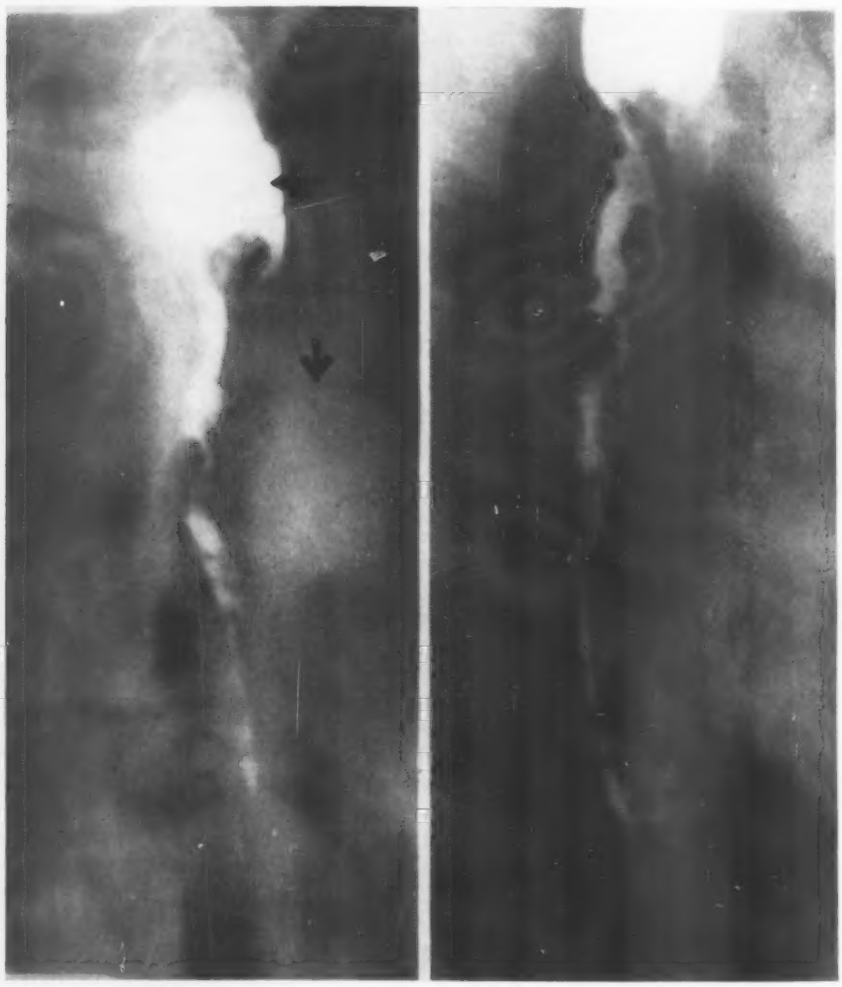


FIG. 1.—Preoperative esophagogram. Defect in the superior mediastinal segment between the level of jugulary notch (arrow) and upper border of aortic arch (arrow).

turned towards his right side, and the whole of the left and left-anterior surfaces of the neck, thorax and upper abdomen exposed and prepared as the operative field. The left arm, wrapped in sterile towels, was supported away from the body at about 45 degrees.

The objective of the first phase of the operation was to determine the operability of the tumor. The incision was made along the anterior border of the left sternocleidomastoid muscle from the level of the hyoid bone to the jugular notch. The muscle was retracted toward the left, and the left lobe of the thyroid toward the right. The middle thyroid vein was ligated and divided, care being taken to leave the lower thyroid artery

intact. The cervical section of the esophagus being exposed, a finger was inserted from the side and introduced into the upper mediastinum in front of the esophagus. The tumor, as well as a mass of nodes to the right of it could be palpated and delineated by blunt dissection. The tip of the finger could then be gently advanced to the posterior surface of the arch of the aorta (Fig. 2). It was found that the tumor could be readily freed from the trachea, and was therefore removable. A pad was placed in the upper mediastinum and the incision temporarily closed with clips.

The patient was then turned to the full right-side position, and the arm supported diagonally upward and forward. An incision was now made along the 6th rib and the rib resected from the costo-vertebral angle to its costal cartilage. The pleural space was found to be obliterated by adhesions which were 5 mm. thick in some places. Only the upper pleural area was in normal condition. The adhesions were broken down, partly by extrapleural pleurolysis so that the lung could retract. After the rib-spreader was placed in position, the entire left pleural cavity could be freely explored and next the mediastinal

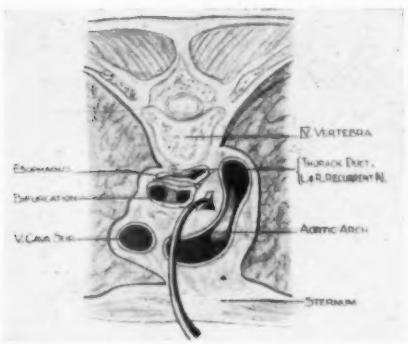


FIG. 2.—Cross-section at the level of the 4th dorsal vertebra. The arrow indicates the paraesophageal space which is explored from the cervical incision in order to determine operability of the tumor.

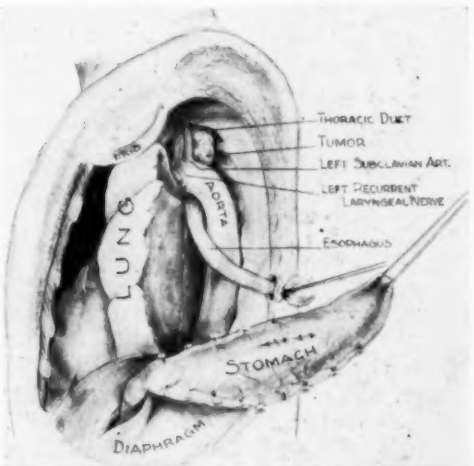


FIG. 3.—The cardia is transsected and inverted after mobilization of esophagus and stomach.

pleura attached to the esophagus was incised both above the aortic arch and below it as far as the cardia. The pad was then removed from the upper mediastinum. The diseased area of the esophagus could then be freed on all sides, without damage to the left recurrent laryngeal nerve or the thoracic duct. The left vagus nerve was identified in the upper angle of the wound, the right vagus nerve remained unexposed.

The esophagus was then freed along the rest of its length, after the vessels supplying it from the aortic arch and aorta had been divided between silver clips. The two Nn. vagi were identified below the tracheal bifurcation and cut. The phrenic nerve was crushed above the diaphragm and then the diaphragm itself was incised from the hiatus almost up to the lateral chest wall, permitting access to the upper abdominal cavity. The stomach was then mobilized in the usual manner after ligation and division of the left gastric artery, the vasa brevia and the left gastro-epiploic vessels. The gastro-colic ligament was divided close to its colonic attachment so that its own blood vessels could be preserved for collaterals to the stomach. The stomach was cleared of all connections as far as the pylorus.

The esophagus was then cut through at its junction with the stomach and the cardia closed with a double row of interrupted silk sutures. The open end of the esophagus was tied off and covered by a rubber cap, fixed in position with a strong silk thread which

was left long (Fig. 3). By means of a long forceps passed through the cervical incision into the mediastinum the free end of the esophagus was grasped and the entire thoracic esophagus was pulled out through the cervical wound.

The uppermost tip of the fundus of the stomach was then equipped with two strong sutures to be used for manipulating the organ. The long ends of these sutures were grasped by the forceps, again introduced through the cervical wound, and the stomach was thus pulled upward between the hilus of the lung and the aortic arch. In this way the stomach had the aortic arch behind it and the hilus in front of it. The transposition of the stomach into the cervical incision was aided by manual support through the open

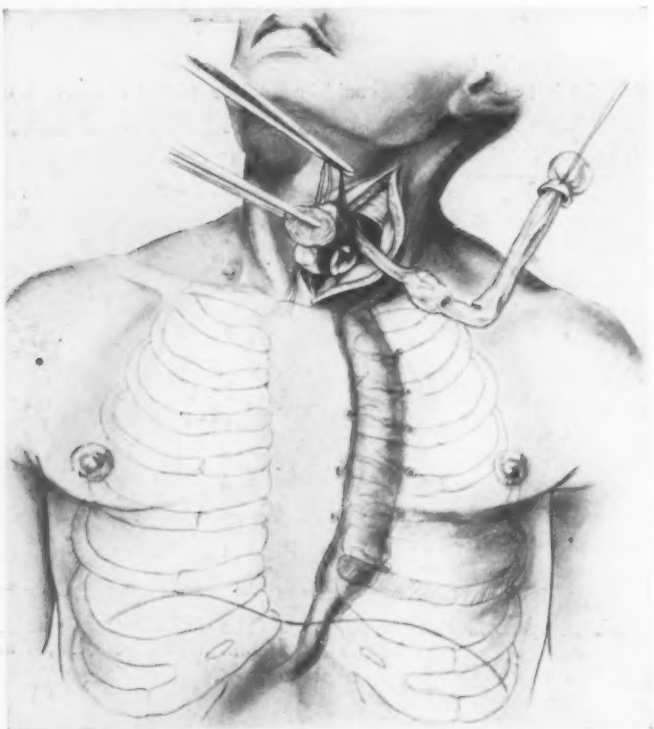


FIG. 4.—The esophagus is pulled out through the cervical incision. The stomach is withdrawn through the lower angle of the same incision and held in this position by 2 guide sutures.

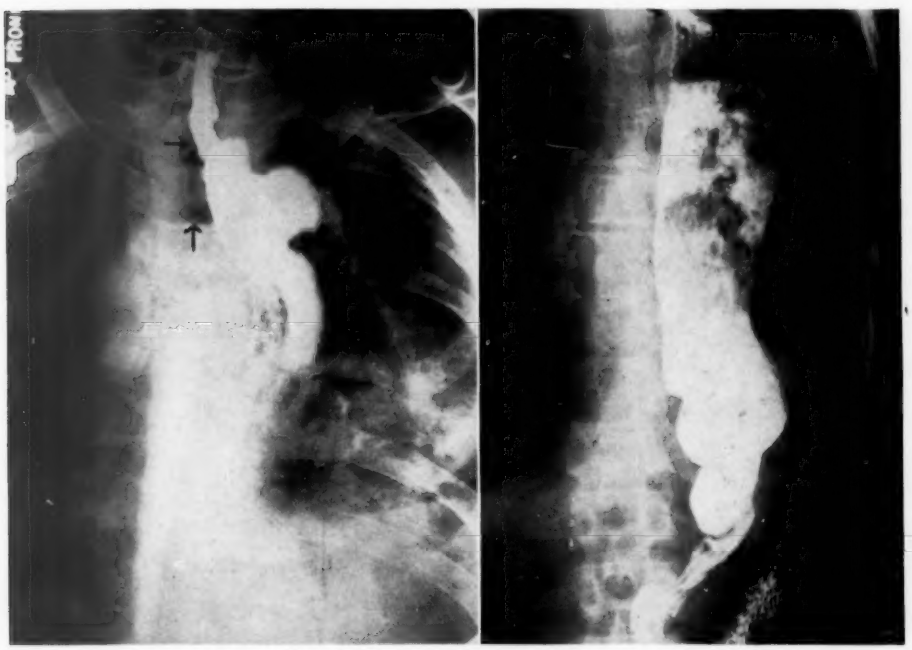
chest cavity, and the fundus could readily be brought up to the level of the larynx. The stomach was held in this position by means of a clamp attached close to the knots of the holding sutures and resting across the line of the neck incision (Fig. 4).

A number of fine silk sutures were used to attach the intrathoracic gastric segment to the mediastinal pleura. At the point where the fundus of the stomach enters the neck area the sutures were placed close together so that the line would be air-tight. Then the incision in the diaphragm was closed by single sutures and centrally its edges were attached to the adjacent prepyloric region of the stomach. Twenty cc. of saline containing 100,000 units of penicillin were divided between mediastinum and pleural cavity.

A medium-sized catheter was now introduced into the chest cavity via a small incision in the ninth intercostal space at the posterior axillary line. The lung was inflated, and the chest incision closed in layers.

The patient was then placed on his back, and the cervical incision reopened. The esophagus was transected 2 cm. above the upper limit of the tumor; the fundus was incised between the two holding sutures and anastomosis made between it and the upper esophagus remnant by means of a double layer of single sutures of fine silk. After the posterior suture line was finished, the anesthetist passed a Levine tube through the nose into esophagus and stomach. The left lobe of the thyroid was used as a covering to reinforce the front of the anastomosis. Two strips of iodoform gauze were inserted towards the mediastinum, and the neck incision closed in two layers.

The duration of the operation was 3½ hours, and up to the last 15 minutes there were no notable fluctuations in pulse or blood-pressure. There was a moderate fall in blood-pressure during the last quarter hour. A blood transfusion was started just before the first incision, and 1500 cc. were given during the operation.



A B

FIG. 5. (A & B)—Postoperative roentgenograms after ingestion of barium. The anastomosis (arrow) is visible above the level of the suprasternal notch. (Arrow)

After the bronchial secretions had been aspirated, the endotracheal tube was withdrawn and the patient was returned to bed under an oxygen tent. The Levine tube was connected with a Wangensteen suction apparatus; the intercostal catheter with an underwater drainage bottle.

The patient regained consciousness after 1½ hours. There had been no damage to the recurrent laryngeal nerves, as his voice was normal. For a time, daily intramuscular injections of penicillin and streptomycin were given. For the first five days parenteral feeding was used exclusively. (2000 cc. of 5 per cent glucose solution were given daily and 500 cc. of blood every second day.) The Levine tube was withdrawn on the fifth day. Oral feeding was begun with 15 cc. of milk every hour and after three more days fluids were permitted as desired. From the tenth postoperative day soft diet was given and swallowing proceeded normally. Drainage through the intercostal catheter ceased on

the third postoperative day, and the tube was removed on the fifth day. The gauze drains were withdrawn from the neck wound on the sixth day.

Roentgen-ray films at the bedside on the third, fifth and eighth days after operation revealed clear lung fields on both sides except for a shadow in the lower left area. A tube-shaped air space, corresponding to the situation of the intrathoracic stomach was plainly visible. The patient was out of bed on the sixth postoperative day.

FIG. 6.—Postoperative roentgenogram of the cervical esophagogastrostomy. Anastomosis and suprasternal notch marked by arrows.

Attacks of expiratory dyspnoea very similar to bronchial asthma occurred from the second to the eighth day after operation. These spells lasted from 10 minutes to as long as three hours accompanied by the characteristic asthmatic wheezing, but uninfluenced by adrenalin and atropin injections. There were no further attacks after the eighth day. During the first few days after operation the pulse rate remained at from 100 to 120, but

returned to normal on the seventh day. For the first ten days the respiratory rate was 22 and 26.

Pathologist's Postoperative Report: The specimen consists of resected portion of esophagus which is already opened and measures 18 cm. in length. One and one-half cm. from one end there is a firm elevated nodular sub-mucosal area which tapers into a constricted portion. This constriction is 4 cm. from one end. Six cm. from this end the mucosa is replaced by yellow tan, firm papillary-like tissue which is continuous with the submucosal layer described above. In an area from 2 to 8 cm. from one end of the esophagus the submucosal tissue is hard and nodular. The mucosa in this area is a greenish red and is firmly adherent to the submucosa. The remainder of the mucosa is tan, gray, and is freely movable. Two lymph nodes 1 cm. in diameter are found at the central portion of the esophagus.

Microscopic Examination: In one area the mucosa is ulcerated. The tumor consists of nests of ovoid or polygonal cells of varying size and shape. In many cells the nuclei are hyperchromic and in a few mitotic figures are present. There are extensive foci of necrosis. The lymph nodes show extensive pigmentation, but no involvement by tumor.

Roentgen-ray pictures taken four weeks postoperative show the new location of the stomach with the esophagogastrostomy above the level of the supra sternal notch (Figs. 5, 6). (See footnote, page 30.)

COMMENT

In our technic of operation there were a few minor deviations from Garlock's description. We resected the sixth rib instead of the seventh in order to have a better approach to the supra aortic space, where preservation of the recurrent nerves and the thoracic duct demand careful dissection and hemostasis under adequate visualization.

No attempt was made to anchor the upper end of the transplanted stomach to the areolar tissue of the jugular notch. The success of the entire procedure must depend in large part upon maintaining an adequate blood supply for the mobilized stomach. We therefore avoided placing any sutures (which might occlude vessels unnecessarily) in the stomach wall, particularly as there was no evidence of increased tension upon the anastomosis.

This "drag" on the anastomosis which is often mentioned in the papers dealing with esophago-gastrostomy seems to be somewhat overstressed. There are cases in which at the end of the operation some tension on the anastomosis is evident, but even in these the usual atonia caused by vagotomy will neutralize the drag in a short time. In one of our patients (carcinoma of the middle third) the anastomosis was under considerable tension. As this patient had had a previous esophagogastrostomy for cardiospasm, the stomach was simply too short to allow relaxation of the tension, although the organ had been well mobilized. When, three weeks following the operation, an esophagogram was taken, we were surprised to find the fundus of the stomach in the dome of the pleura, its cranial end at a higher level than the anastomosis.

Preservation of the cervical and upper thoracic portions of the Nn. vagi is obviously a prerequisite for a satisfactory outcome. As noted in the description of the operation, we cut the nerves well beyond the level of the bifurcation of the trachea so as to save those branches joining the pulmonary plexus.

Garlock believes that "vagal stimulation" was the cause of death in his patient. But it is questionable, whether a protracted vagal reflex ever does occur. During the operation mentioned by Garlock, pulse, blood pressure and respiratory rate remained undisturbed. There was thus no evidence of hyperstimulation of the vagi while the dissection in the vicinity of the nerves was being performed. It seems unlikely that any marked degree of irritation of the vagi would develop after completion of the operation.

On the other hand late fatal effects are well known as a consequence of vagal *paralysis*. In fact, bilateral vagotomy at a high level is always fatal in

FIG. 7 FIG. 8

FIGS. 7 and 8.—Photographs of patient 6 weeks after operation. Neck incision and thoracic incision visible.

experimental animals, as is confirmed in the physiological literature. In these experiments bilateral vagotomy was routinely done at the cervical portion of the nerves, and the simultaneous paralysis of the laryngeal recurrents was believed to be the cause of the fatal pneumonia. Other theories emphasize the inability of glycogen synthesis in the liver following vagotomy which in turn may seriously impair the nutritional condition of the heart muscle. In experiments on dogs, we[2] found sufficient proof to assume that maintenance of the pH equilibrium in the blood is dependent on intact cervical portions of the vagi nerves. After bilateral vagotomy an irreversible and therefore fatal acidosis by CO_2 accumulation in the blood developed.

Attempts to replace the entire thoracic esophagus by the mobilized stomach are not new. As far back as 1920 Kirschner[3] was successful in performing a cervical esophagogastrostomy on a patient with cicatricial stenosis of the mediastinal part of the esophagus. No resection, however, was done. Kirschner divided the stomach close to the cardia and performed an anastomosis between cardia and jejunum. The stomach was then mobilized in the same way as has become today's routine procedure, and was brought up to the neck through a subcutaneous tunnel on the anterior chest wall. The cervical esophagus was exposed and connected with the fundus of the stomach by side-to-side anastomosis. The patient survived. Kirschner thought it an advantage to avoid the transpleural route. H. Kuemmell Jr.[4] advised a similar method. He freed the thoracic esophagus through the hiatus esophagus and a left cervical incision by blunt and blind dissection. The stomach was then devascularized according to Kirschner and pulled up to the neck. None of Kuemmell's patients survived.

The first case of successful cervical esophagogastrostomy following resection of an upper third cancer was reported by Sweet[5] in December, 1948. (Operation on October 28, 1947.) Sweet started with the thoraco-abdominal part of the operation, turned the patient on his back and performed the anastomosis from a combined thoraco-cervical incision. He thought it necessary to remove the mesial part of the left clavicle, the prominent corner of the manubrium of the sternum, and the anterior half of the first rib. A previous attempt to pull the stomach up through the apex of the thorax into the base of the neck had apparently failed because of insufficient room to perform an anastomosis. It may be assumed that Sweet had to deal with an abnormally narrow aperture. We did not experience any difficulty in bringing the stomach through the aperture. There was even room enough to place two packs beside the end of the stomach. This is understandable, for we know that the lower lobes of the thyroid gland often grow down into the upper mediastinum without causing pressure symptoms. In the average case Garlock's procedure seems to be preferable, because it is the simpler one.

Data as to the after effects of cervical esophagogastrostomy are beginning to be recorded. Garlock himself interpreted the significance of the fatal outcome of his case as probably connected with some changes in the vagal mechanism secondary to operation. Sweet noticed that turning his patient on the left side was followed by rapid pulse and marked fall in blood pressure. Both signs disappeared when he was turned back again. This was thought to be caused by stimulation of the carotid sinus.

In our case a postoperative complication was an asthmatic condition lasting for five days, and uninfluenced by atropin and adrenalin. Asthmatic attacks had not occurred previously. The expiratory dyspnea itself was not serious, but the accompanying cough—though rather unproductive—caused regurgitation of gastric content. Factors probably responsible for this are: the high level of the anastomosis adjacent to the pharynx; the absence of a sphinc-

ter mechanism; and the atonic state of the stomach because of vagotomy. Thus the stomach is exposed to the oscillations of the intrapleural pressure which becomes strongly positive during the cough effort. The relation of the attacks of bronchial asthma to the operative procedure is problematical. Vagal *and* sympathetic nerves both are said to participate in the innervation of the muscles of the bronchial wall. Surgical treatment of bronchial asthma has been tried by means of sympathectomy and vagotomy. The reported percentages of alleged improvements are about the same, whether sympathectomy or vagotomy was performed.

SUMMARY

A case of cervical esophago-gastrostomy following resection of a supra-aortic carcinoma of the esophagus is reported. The satisfactory outcome of the operation indicates the justification of a combined cervico-thoracic approach as recommended by Garlock.

The rôle of the Nn. vagi in postoperative disturbances is discussed.

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(Footnote to case report ending on page 27.) The last follow-up examination occurred June 20, 1949. Normal swallowing function (confirmed by roentgenogram) was noted. General condition is satisfactory.

SURGICAL TREATMENT OF DUODENAL ULCER — COMPARISON OF RESULTS WITH AND WITHOUT VAGOTOMY*

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WE ARE REPORTING the results of surgical treatment of 174 cases of intractable duodenal ulcer. The first half of the series had gastric resections or gastro-enterostomies and the second half had vagotomies with pyloroplasty or gastro-enterostomies. Both series are similar in respect to average age, duration of symptoms, preoperative complications and severity of the disease. The same two surgeons performed the operation in both groups. The period of study was from January, 1942, to January, 1948.

TYPE OF OPERATION

The first 87 patients in the series were subjected to gastric resection or gastro-enterostomy. Sixty-seven of these had the distal two-thirds of their stomachs resected and continuity restored by a short-loop retrocolic gastro-jejunostomy, with the distal end of the jejunum directed to the greater curvature of the stomach. Hoffmeister's modification of the posterior Polya technic was employed.

Twenty patients were treated by posterior gastro-enterostomy with the jejunal loop attached to the stomach in an antiperistaltic direction. The cases selected for gastro-enterostomy were usually obstructing ulcers in older patients, active ulcers in patients whose condition was such that the risk of resection was too great, or penetrating ulcers in which the technical difficulties of resection would have increased the risk.

The second half of the series is composed of 87 consecutive cases in which transabdominal vagotomy was employed in conjunction with either pyloroplasty or gastro-enterostomy. The pyloroplasty consisted merely in longitudinal division and transverse suture of the pylorus, occasionally with excision of an ulcer on the anterior wall of the duodenum. Gastro-enterostomy was performed by the same technic as in the first series.

INDICATIONS FOR OPERATION

Patients with duodenal ulcer were not operated upon unless they proved intractable to medical management. The indications for operation were the same in the second group as in the first (Table I).

COMPARISON OF THE POSTOPERATIVE FOLLOW-UP

Since none of the patients in the second group have been followed longer than 18 months, care was taken to disregard any symptoms in the first group which appeared more than 18 months after operation. Thus, if a patient had

* Submitted for publication, December, 1948.

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had a gastric resection and was well at the end of one year, he would be classified in this study as well, even if he developed a marginal ulcer two years later.

In the first group frequent feedings and antacids were advised and smoking and drinking were prohibited, whereas the patients subjected to vagotomy were given no dietary or medical management after the sixth week and were allowed to smoke or drink if they so desired.

A factor which may influence the statistics is the fact that the patients subjected to vagotomy were questioned routinely about diarrhea and vomiting. If the patient vomited only once or twice or had two or three stools a day, it

TABLE I.

	Gastric Resection or G. E.	Vagotomy with Pyloroplasty or G. E.
Total consecutive cases	87	87
Total followed cases	76	83
Duration of follow-up	5 to 18 mo. av.—11 mo.	5 to 18 mo. av.—14 mo.
Average age	44 1 yrs.	47.3 yrs.
Duration of symptoms	11.9 yrs.	12.5 yrs.
Duodenal ulcer demonstrated at operation	87	87
Intractable epigastric pain	87	87
Night pain	20	19
Hemorrhage	29 (Multiple 15)	29 (Multiple 9)
History of perforation	6	8 (Multiple 2)
Pyloric obstruction	29	27

was recorded, whereas minor episodes of diarrhea or vomiting which occurred after gastric resection might not have been recorded at the time and might subsequently have been forgotten by the patient.

POSTOPERATIVE COURSE

In general, the postoperative course of the patients with vagotomy and pyloroplasty or gastro-enterostomy was little different from that of the patients with gastric resection or gastro-enterostomy alone. The hospital mortality was lower in the patients subjected to vagotomy than in the first group. There were two deaths after gastric resection and one after gastro-enterostomy alone compared with only one death in the patients with vagotomy.

PERSISTENCE OR RECURRENCE OF ULCER PAIN

There was a striking difference in the two groups regarding control of ulcerlike pain. Ulcerlike distress often persisted after gastric resection or after gastro-enterostomy and required dietary management or antacids but was rarely observed after vagotomy.

TABLE II.—*Recurrence of Ulcer Pain Since Operation.*

Resection or G. E.		Vagotomy and G. E. or Pyloroplasty	
Yes	18	Yes	4
No	55	No	79

PERSISTENCE OF ABDOMINAL PAIN OTHER THAN ULCERLIKE PAIN

All types of pain, except ulcerlike distress, are included in this category and are about equally common in the two groups. Incisional pain was the commonest. Lower abdominal pain, perhaps referable to the colon, was observed in both groups but was less common in the patients subjected to vagotomy.

TABLE III.—*Abdominal Pain Other Than Ulcer Pain Since Operation.*

Resection or G. E.		Vagotomy and G. E. or Pyloroplasty	
Yes	20	Yes	20
No	55	No	63

VOMITING

Only two of the patients subjected to pyloroplasty or gastro-enterostomy coupled with vagotomy vomited enough to cause concern. Mild vomiting is defined as not over five times since operation; severe as more than five times. The severity of the vomiting in the first series cannot be estimated accurately because the number of times that the patients vomited was not recorded at the time and memory is not reliable.

TABLE IV.—*Vomiting Since Operation.*

Resection or G. E.		Vagotomy and G. E. or Pyloroplasty	
Yes	7	Yes: Repeatedly	2
		Occasionally (1 to 6 times a year)	15
No	66	No	66

DIARRHEA

Only two patients subjected to vagotomy had troublesome diarrhea, which persisted for more than five months. Five patients in the first group complained of diarrhea of varying degrees of severity. Constipation was also a complaint in a number of cases in both groups. Transitory diarrhea was seen more often in the patients with vagotomies than in the first group.

TABLE V.—*Diarrhea Since Operation.*

Resection or G. E.		Vagotomy and G. E. or Pyloroplasty		
Yes	5	Yes	2	(5 to 10 stools daily)
			11	(Transient for 6 weeks after operation)
			17	(Occasionally mild—1 to 5 stools daily)
		Total	30	
No	67	No	53	

FEELING OF WELL-BEING

Table VI refers to all complaints referable to any system of the body and includes such symptoms as backache and headache. The question was designed

to evaluate the status of the patient as a whole rather than that of the gastro-intestinal tract. The patients with vagotomies had fewer complaints than those in the first group. There appeared to be little difference in the two groups as to the length of time before returning to work.

TABLE VI.—*Do You Consider Yourself Well?*

Resection or G.E.		Vagotomy and G. E. or Pyloroplasty	
Yes	48	Yes	58
No	20	No	19
Improved	2	Improved	4

DEMONSTRABLE RECURRENT ULCERATION

Two of the three demonstrable jejunal ulcers which occurred in the gastric-resection, gastro-enterostomy group occurred after resections. Three of the four hemorrhages in this group occurred after gastro-enterostomy.

In only one case in the vagotomy group has there been any objective evidence of recurrent ulceration demonstrable by either roentgen ray, gastroscopy, or by such clinical signs as hemorrhage or perforation. This patient was classified at the end of five months as a failure because ulcerlike pain had persisted, unrelieved by gastro-enterostomy and vagotomy. Eight months after operation a jejunal ulcer was demonstrated. Three additional vagus fibers were found, divided and confirmed by histologic examination. The pain which before reoperation had required morphine was relieved at once, but it recurred within three weeks. The gastro-enterostomy was taken down, the jejunal ulcer excised, and a pyloroplasty was performed. After operation the insulin-tolerance test showed clear evidence that the vagotomy was still incomplete. The patient's symptoms have been controlled by a course of roentgenotherapy to the stomach, enterogastrone, antacids and diet. The patient's hypersensitive personality, and his symptoms, suggesting a dump syndrome, even with gastro-enterostomy, influenced our decision to perform a pyloroplasty rather than to resect the stomach.

TABLE VII.—*Objective Evidence of Recurrent Ulceration.*

Resection or G. E.		Vagotomy and G. E. or Pyloroplasty	
Proved jejunal ulcer 2 after gastric resections 1 after G. E.	3	Proved jejunal ulcer	1
Hemorrhage 1 after resection 3 after G. E.	4	Hemorrhage	0

EVALUATION OF RESULTS

The criteria used in evaluating the results were shown in Table VIII. Although the group of cases subjected to gastro-enterostomy alone is

small, the difference between the results obtained in this group and those following gastro-enterostomy combined with vagotomy is striking enough to indicate that the excellent results obtained following gastro-enterostomy and vagotomy are not attributable to the gastro-enterostomy alone.*

TABLE VIII.

Excellent	— 100% normal health from gastro-intestinal standpoint.
Satisfactory	— No ulcer distress, gastro-intestinal symptoms so mild that they do not interfere with work; no special diet or medication recommended or taken.
Improved	— No ulcer distress, fewer gastro-intestinal symptoms than before operation, but diet and/or medication have been used to control symptoms.
Failure	— Persistence of ulcerlike distress or development of other gastro-intestinal symptoms sufficiently severe to constitute a disability.

The results obtained following gastric resection alone and following G. E. alone are shown in Table X.

DISCUSSION

Some surgeons performing 100 operations for duodenal ulcers will perform 50 gastric resections and 50 gastro-enterostomies whereas others may perform 90 resections and 10 gastro-enterostomies. The reasons for selecting one operation or the other depend on the type of ulcer, the condition of the patient and the risk of operation. In evaluating the efficacy of a new procedure, it is not fair to compare it with only a selected group of cases

TABLE IX.—*Comparison of Results in 156 Cases Followed From 5 to 18 Months After Operation.*

Operation	Excellent	Satisfactory	Improved	Failure
Vagotomy with gastro-enterostomy or pyloroplasty, 83 followed cases*	78%	11%	5%	6%
Gastric resection, 57 cases	60%	10%	4%	26%
Gastro-enterostomy, 16 cases				
Total, 73 followed cases				

treated by gastric resection. For this reason the results obtained following vagotomy combined with a shunt operation should not be compared with the results obtained following gastric resection alone or following gastro-enterostomy alone, but should be compared with an equal number of consecutive cases in which the patients were operated upon by the old technics, including both gastric resections and gastro-enterostomies.

If a surgeon who is accustomed to performing gastric resections for duodenal ulcer begins to employ vagotomy, his tendency is to employ vagotomy at first in the milder cases and to rely on time-tested gastric resection to control the complicated ulcers. Consequently, he may employ vagotomy in some cases in which the objective findings are not proportionate to the subjective, and use it in a selected group of cases whose symptoms are more

* There was no significant difference in the results following vagotomy and gastro-enterostomy as compared with vagotomy and pyloroplasty.

the result of functional disorders than of organic disease. Since vagotomy does not benefit functional gastric distress or symptoms due to gastritis, he may find that the results in his selected group of cases are poor.

The cases reported here are not selected but are consecutive. After experience in the technic had been gained by operations on a number of jejunal ulcers, the decision was made to employ vagotomy in the treatment of all duodenal ulcers, and from that time no further gastric resections were employed. Nor were vagotomies employed in the treatment of duodenal ulcer during the period of time that gastric resections were being done. For these reasons both series represent a consecutive, not a selected, group of cases.

In this series the criteria for operation, the severity of the disease and the surgeons performing the operations were the same. The period of follow-up is the same and the percentage of patients followed is comparable. Although the series is small, the differences in results appear to be significant.

TABLE X.

Operation	Excellent	Satisfactory	Improved	Failure
Gastric resection, 57 cases	67%	10%	4%	19%
Gastro-enterostomy, 16 cases	38%	6%	6%	50%

The mortality rate for the vagotomy group is lower than for the group treated by gastric resection or gastro-enterostomy alone. The side effects following vagotomy were of minor importance and were comparable, in most respects, to the side effects following gastro-enterostomy without vagotomy. Even those patients who developed side effects following vagotomy were glad that the operation had been performed and were well pleased with their improvement. Persistence of the symptoms of ulcer and demonstrable recurrences of ulcer were much lower in the vagotomy group. Finally, the number of patients who considered themselves entirely well and the number of patients whose results were objectively classified as excellent were higher in the group subjected to vagotomy.

SUMMARY

1. A series of 174 cases of intractable duodenal ulcer treated by various types of operation is reported.

2. This series is composed of two groups of 87 patients each. In the first group 67 patients were treated by gastric resection and 20 by gastro-enterostomy. In the second group all patients were treated by pyloroplasty or gastro-enterostomy coupled with vagotomy.

3. The two series are similar in respect to average age, duration of symptoms, preoperative complications and severity of the disease. The same two surgeons performed all operations in both groups. The mortality rate in the vagotomy series was 1.1 per cent as compared to 3.4 per cent in the patients subjected to gastro-enterostomy or gastric resection.

4. On the basis of our experience, vagotomy with gastro-enterostomy or pyloroplasty has the following advantages over gastric resection or gastro-enterostomy:

a. a lower mortality rate.
b. a lower incidence of demonstrable recurrent ulceration.
c. a lower incidence of recurrent gastro-intestinal hemorrhage.
d. a lower incidence of recurrent ulcer pain.
e. a lower incidence of abdominal pain of all types.

5. Vagotomy with gastro-enterostomy or pyloroplasty has the following disadvantages:

a. a possible greater incidence of transitory postoperative vomiting.
b. a probable greater incidence of transitory postoperative diarrhea.

6. Although the results following gastric resection are superior to those following gastro-enterostomy, even the selected patients (67 of 87) whose stomachs were resected had a significantly higher mortality and morbidity after operation than did those subjected to vagotomy coupled with gastro-enterostomy or pyloroplasty.

7. The side effects of vagotomy have been few and mild.

CONCLUSION

In the first 18 months after operation, vagotomy, in conjunction with gastro-enterostomy or pyloroplasty, has given better results than gastric resection or gastro-enterostomy alone.

"CATEGORICALLY INOPERABLE" CARCINOMA OF THE BREAST*

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SUCCESSFUL TREATMENT of cancer of the breast can only be accomplished by radical mastectomy. This procedure today is essentially the same as that described by Halsted. Many technical variations have appeared throughout the years, but with little if any improvement in clinical results.

For the most part, the procedure of radical mastectomy has been advised for all patients in which the operation was a technical possibility.

In general, the criteria of operability have been:

1. Movable primary tumor.
2. Limitation of the metastases to the axilla of the same side as the primary tumor (checked by roentgenograms of chest and skeleton).
3. Movable metastases.

While these criteria may satisfy the technical requirements for radical mastectomy, the clinical results leave much to be desired.

This discrepancy between technical operability and clinical curability was very forcibly demonstrated in an excellent series of papers by Haagensen and Stout.[1, 2, 3] Following a very critical review of the cases of breast carcinoma seen at the Presbyterian Hospital in New York, they came to the conclusion that the clinical results did not justify the procedure of radical mastectomy in many cases in which the operation was technically possible. They further concluded that the "categorically inoperable" cases could be readily identified by certain definite signs of the advancement of the disease. They accordingly drew up the following rule for judging the operability of breast carcinoma:

Women of all age groups, who are in good enough general condition to run the risk of major surgery should be treated by radical mastectomy, except as follows:

1. When the carcinoma is one which developed during pregnancy or lactation.
2. When extensive edema of the skin over the breast is present.
3. When satellite nodules are present in the skin over the breast.
4. When intercostal or parasternal tumor nodules are present.
5. When there is edema of the arm.
6. When proved supraclavicular metastases are present.
7. When the carcinoma is the inflammatory type.

* Submitted for publication, November, 1948.

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8. When distant metastases are demonstrated.
9. When any two, or more, of the following signs of locally advanced carcinoma are present:
   a. Ulceration of the skin.
   b. Edema of the skin of limited extent (less than one-third of the skin over the breast involved).
   c. Fixation of the tumor to the chest wall.
   d. Axillary lymph nodes measuring 2.5 cm. or more in transverse diameter and proved to contain metastases by biopsy.
   e. Fixation of axillary lymph nodes to the skin or the deep structures of the axilla, and proved to contain metastases by biopsy.

These investigators found 109 cases in their series which met these criteria of inoperability. Of this group, there were no permanent cures. Three cases remained clinically free of metastases for as long as five years but later died of

TABLE I.—*Signs of Locally Advanced Carcinoma of Breast.*

	No. of Patients
Inflammatory type of carcinoma	6
Satellite nodules	23
Pigskin appearance over one-third of the breast	35
Supraclavicular nodes	18
Edema of arm	3
Distant metastasis	5
Pregnancy and lactation	3
Lymph nodes in axilla 2.5 cm. or more in transverse diameter along with some other sign of locally advanced carcinoma	19
Ulceration of skin along with some other sign of locally advanced carcinoma	37
Fixed axillary nodes with some other sign of locally advanced carcinoma	3
Fixation to chest wall with some other sign of locally advanced carcinoma	4
Pigskin appearance of less than one-third of the breast with some other sign of locally advanced carcinoma	16

recurrent or metastatic carcinoma. They also presented evidence which suggested to them that if these cases, classed as categorically inoperable, were subjected to radical mastectomy, their life expectancy was shortened by about 10 months (as compared with similar untreated cases).

It was our purpose to apply these same criteria of inoperability to a group of cases of breast carcinoma (female) from the Barnard Free Skin and Cancer Hospital. We therefore reviewed all cases of carcinoma of the breast seen from 1933 to 1943, inclusive. We found 167 cases which fell into the categorically inoperable group. Of these, 100 were treated by the routine radical mastectomy or some similar radical operative procedure, and the remaining 67 were treated only by roentgen-ray.

In Table I we have classified these 100 operative cases according to the category of inoperability into which they fell.

It is obvious from Table I that many of these patients were categorically inoperable because of two or more signs of advanced carcinoma.

In Table II we have listed the various forms of therapy used in these cases. All consisted of some form of mastectomy.

Of the 100 cases which had one of the radical operative procedures as shown in Table II, only two were well and clinically free of carcinoma at the

end of five years; one for 8 years, and the other for 14 years. Both of these survivals were those in the category of a carcinoma of the breast associated with pregnancy or lactation. Inasmuch as our series contained a total of but three cases in this category, we consider these two survivals rather important, and therefore include the following brief clinical records of each.

CASE HISTORIES

M. B., Hospital No. 78734. A 40-year-old white female, who had had 12 previous pregnancies, three of which terminated in spontaneous abortions, was first seen in the Barnard Hospital dispensary November 20, 1939. At that time she was diagnosed clinically as having carcinoma of the left breast, with axillary metastasis. She was advised to enter the hospital for radical mastectomy. This she refused, and in February, 1940,

TABLE II.—*Type of Treatment.*

	No. of Patients
1. Radical mastectomy with knife	34
2. Radical mastectomy with knife plus routine postoperative roentgenotherapy	10
3. Radical mastectomy with knife plus irradiation when signs of recurrence appear	21
4. Simple mastectomy with knife plus routine postoperative roentgenotherapy	5
5. Preoperative roentgenotherapy plus radical mastectomy with knife plus roentgen treatment when signs of recurrence appear	3
6. Preoperative roentgen-ray plus radical mastectomy plus routine postoperative roentgenotherapy	5
7. Preoperative roentgenotherapy plus simple mastectomy plus routine postoperative roentgen treatment	1
8. Preoperative roentgenotherapy plus radical mastectomy	6
9. Simple mastectomy with actual cautery	1
10. Radical mastectomy plus routine postoperative roentgenotherapy including roentgen castration	1
11. Shoulder-girdle amputation	1
12. Radical mastectomy with actual cautery	4
13. Radical mastectomy with knife plus roentgen castration	1
14. Simple mastectomy plus axillary-gland dissection (pectoral muscles left intact)	1
15. Radical mastectomy with actual cautery plus routine postoperative roentgenotherapy	1
16. Radical mastectomy with actual cautery plus roentgenotherapy when signs of recurrence appear	3
17. Preoperative roentgenotherapy plus radical mastectomy including supraclavicular dissection	1
18. Radical mastectomy with knife plus supraclavicular dissection	1

became pregnant. In May, 1940, she had a spontaneous abortion. In October, 1940, she was admitted to the hospital and had a left radical mastectomy—11 months after the original diagnosis. The pathologic diagnosis was adenocarcinoma of the left breast, with axillary lymph-node metastasis. She was last seen on October 26, 1948, at which time she showed no signs of local recurrence or metastasis of the carcinoma.

A. N., Hospital No. 57664. A 37-year-old white female, who had had 14 previous pregnancies, two of which terminated in spontaneous abortions, and one in a stillbirth. She was first seen in the Barnard Hospital dispensary April 18, 1934. Her baby was two months old and she had developed a lump in her right breast two months before the baby was born. Seven weeks before the patient came to the dispensary the baby was weaned. On May 15, 1934, three months after the birth of her child, she had a right radical mastectomy. The pathologic diagnosis was adenocarcinoma of the right breast, with axillary lymph-node metastasis. Eighteen months after the operation, she gave birth to another full-term child. She was last seen April 6, 1948, at which time there were no signs of local recurrence or metastasis of the breast carcinoma.

The question of whether or not patients with categorically inoperable carcinoma of the breast actually have their lives shortened by radical mastectomy is an important one. Haagensen and Stout believe that the life expectancy is materially shortened in the majority of instances. This is based on their figures comparing the length of life of the categorically inoperable cases who had radical mastectomy with a group of untreated carcinomas of the breast. The survival time is figured from the onset of symptoms to the time of death.

In Table III we have compared the total duration of the disease in our two groups of cases with those of Haagensen and Stout. Also included are figures from various groups of untreated cases.[4]

TABLE III.—*Mean Total Duration of Breast Carcinoma—Onset to Death—in Various Groups of Cases.*

A. Wyard	273	untreated cases	39.6	mean duration in months
Lazarus-Barlow	243	untreated cases	39.8	mean duration in months
Daland	100	untreated cases	40.5	mean duration in months
Beatson	61	untreated cases	36.5	mean duration in months
Powell White	59	untreated cases	32.1	mean duration in months
Leeds	26	untreated cases	32.46	mean duration in months
Carter-Braine	15	untreated cases	30.2	mean duration in months
Total	777	untreated cases	38.55	Average
B. 118 Presbyterian Hospital cases regarded as inoperable and denied surgery and irradiation				42.3 months
C. 104 Presbyterian Hospital cases regarded as operable and treated by radical mastectomy, but now classified as inoperable according to Haagensen-Stout criteria				32.3 months
D. 100 Barnard Free Skin and Cancer Hospital cases regarded as inoperable by the Haagensen-Stout criteria who had the type of treatment shown in Table II				36.3 months
E. 67 Barnard Free Skin and Cancer Hospital cases regarded as inoperable by the Haagensen-Stout criteria who had roentgenotherapy alone				34.2 months

DISCUSSION

Throughout the years, thousands of cases of carcinoma of the breast have been reported. These cases have at times been grouped according to rather elastic classifications as to the anatomic, pathologic or clinical degree of the disease. We feel that Haagensen and Stout have described definite signs of the advancement of carcinoma of the breast so conclusively that any worker in this field could use their classification with considerable accuracy. The various series of statistics in breast malignancy would certainly be more comparable if they were grouped according to these standards.

The question of whether or not a category of inoperability, in technically operable cases, is justifiable, is of extreme importance. The fact that we had only two possible cures in our series certainly indicates the poor results which can be expected from patients falling into this category. Strangely enough, both of these survivals were in cases associated with pregnancy. Harrington[5] reports more encouraging results in the treatment of cancer of the breast in the course of pregnancy or lactation. Haagensen[6] also recently pointed out that "it may be that our (Haagensen and Stout) group of cases was a particularly

unfortunate one, and that radical mastectomy is justified in these patients, provided, of course, that the disease is locally operable."

The 36.3 months average survival of our operated cases is quite close to that of 32.3 months of these reported from the Presbyterian Hospital. The Barnard cases treated by roentgen-ray alone had an average survival of 34.2 months. This is somewhat shorter than the Presbyterian Hospital cases, which were denied surgery and radiation (42.3 months).

Thus we may say that, as a rule, cases of breast malignancy which fall into the Haagensen-Stout category of inoperability will not profit by radical surgery. At this time cases of breast cancer occurring during pregnancy or lactation may be an exception to the rule. It is also possible that other criteria of inoperability may be proved to be questionable. However, only by classifying cases against definite standards of involvement will it be possible to arrive ultimately at certain standards of the most beneficial treatment.

SUMMARY

1. The survival rates of 167 cases of carcinoma of the breast, categorically inoperable according to the classification of Haagensen and Stout, have been studied.

2. Of the 100 cases which were treated primarily by some form of mastectomy, only two were alive and well after five years. Both of these cases were of cancer of the breast associated with pregnancy. The average survival time of these 100 cases was 36.3 months.

3. Only groups of cases reported according to standardized anatomic, clinical and pathologic signs of advancement of the disease have any real value.

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EXTERIORIZATION OF THE CANINE VESICAL TRIGONE FOR EXPERIMENTS ON THE KIDNEY*

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INTRODUCTION

It has been necessary to exteriorize the vesical trigone for comparison of clearances by the denervated, transplanted kidney with the intact control in trained unanesthetised dogs (Maluf, 1943). During the past year we have exteriorized, successfully, the trigones of over 20 dogs and the technic has been standardized.

Exteriorization of the trigone may be essential to the success of certain experiments:

1. It permits collection of urine from each ureter of unanesthetised animals. Catheterization of the ureters of unanesthetized dogs by cystoscopy is difficult if not, at times, impossible. In the male dog this is impossible with extant equipment. When a ureter is catheterized, even once, urine is apt to trickle around the ureteral catheter and thus vitiate quantitative collection. Furthermore, ureteral catheterization may evoke reflex vascular changes in the kidney and is likely to introduce infection.

2. The test kidney can be simultaneously compared with the control as standard. One may observe the effects of drugs on a denervated kidney as compared with the control, or may study the results of surgical procedures or various stimuli on one kidney as compared with the control (Maluf, 1949a).

3. One can actually see immediate changes in urinary flow such as may occur under conditions which result in anuria or its relief; for example, in shock, during recovery from shock, during intravenous hemoglobin infusions in states of dehydration or shock and during infusions from other intravenous drips.

4. Urine can be collected quantitatively during short intervals, such as five minutes.

MATERIAL

Only female dogs were used. Males would necessitate total resection of the penis and thus complicate the procedure. Short-haired dogs were preferred because the urine would not be as likely to excoriate, as with long-haired animals.

PROCEDURE

Anesthesia was by intravenous sodium pentobarbital (from 30 to 32 mg./Kg.). The skin of the groins, the inner thighs, the suprapubic region, and the lower half of the abdomen is shaved without abrasion so as to reduce

* Submitted for publication, October, 1948.

subsequent cutaneous complications from urine. Cleansing is done gently with acetone and then aqueous zephiran, 1:1,000. Asepsis is preserved.

The ureters, bladder and most of the urethra of the dog are intraperitoneal organs (Fig. 3). The meso-ureter fuses with the meso-uterus and mesovagina

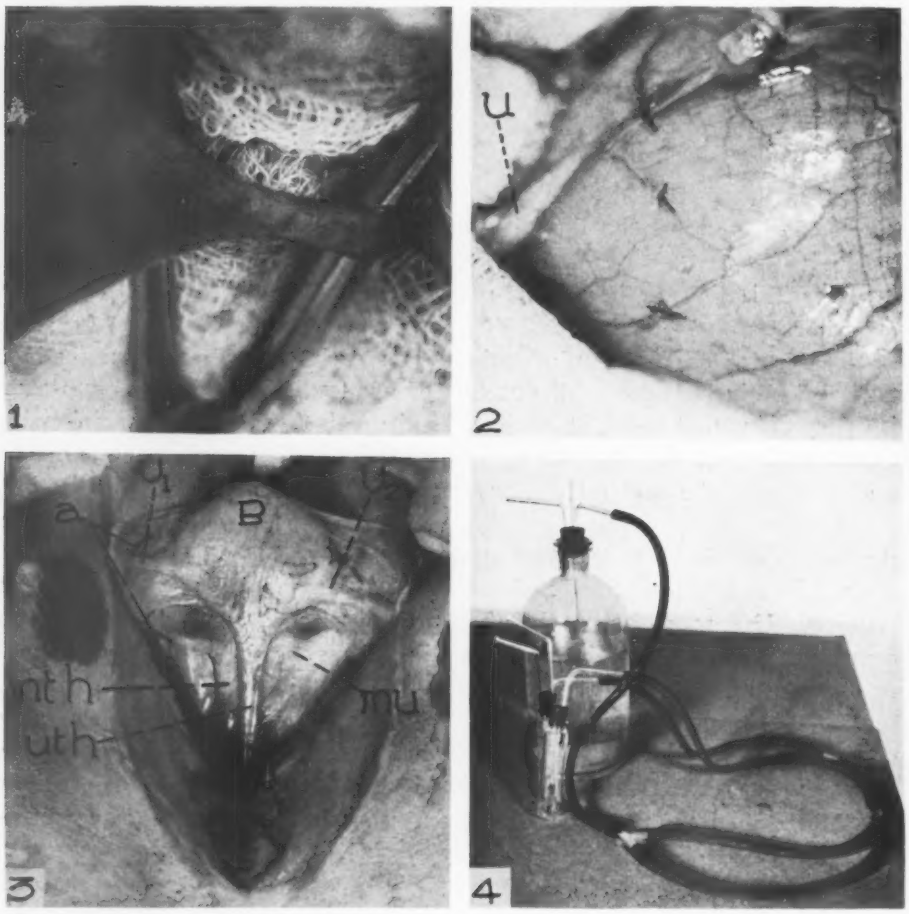


FIG. 1.—The intra-abdominal portion of the urethra fully mobilized prior to its ligation and division at the caudal end. The caudal end is at the right.

FIG. 2.—Bladder partly distended and reflected caudad (toward the right of the picture), showing the right ureter, *u*, entering the bladder (at the left of the picture) and fine ligatures applied to the longitudinal blood vessels about 2 cm. from the entrance of the ureters.

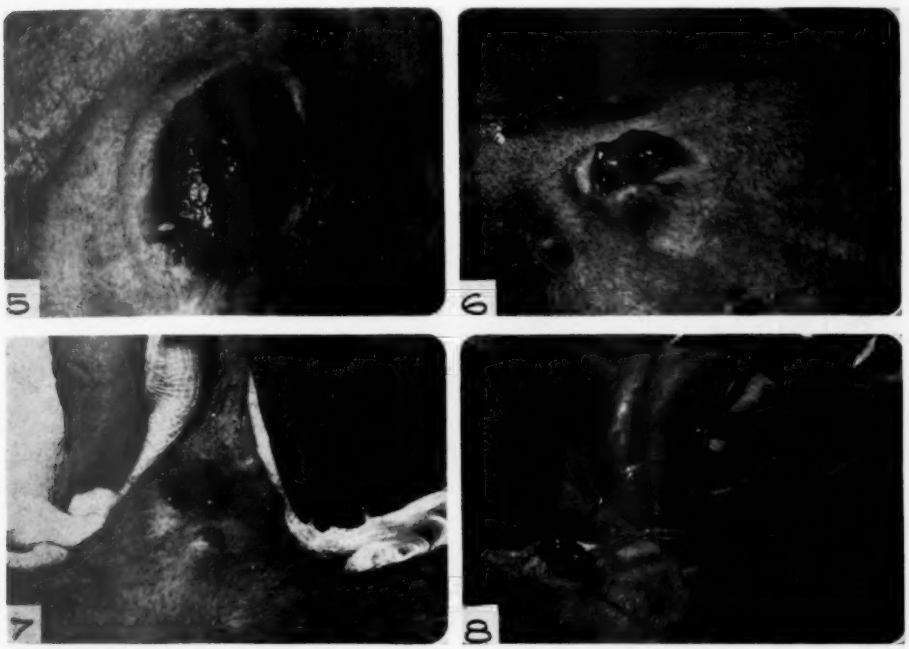
FIG. 3.—Lower urinary tract of a female dog exposed to advantage. *B*, bladder; U_1 *and* U_2, ureters; *uth*. urethra; *mu*, meso-ureter; *mth*, meso-urethra; *a*, arteries to the bladder.

FIG. 4.—Equipment for collection of urine. Suction is applied in the direction of the arrow.

dorsally. The meso-urethra arises bilaterally from each dorsolateral margin of the urethra and is continuous with the meso-ureter. The arteries to the bladder, which are branches of the inferior mesenteric artery and of the

internal pudendal branch of the hypogastric, pass to the bladder in the meso-ureter (Fig. 3).

The median longitudinal abdominal incision, from 8 to 10 cm. long, extends caudad to the pubic symphysis. The bladder, usually partially distended with urine, is delivered through the wound. The practically bloodless urachus, which joins the ventral median surface of the bladder to the umbilicus and to the midline of the ventral abdominal wall caudal to the umbilicus, is divided. The ureters are identified and the membrane with free border, which extends between ureter and bladder (Fig. 1) and which carries a vesical branch of the hypogastric artery, is divided between clamps close to the



FIGS. 5, 6 and 7.—The exteriorized vesical trigone with the adjacent central portion of the bladder and the urethra in three dogs.
FIG. 8.—Collection of urine from the external ureteral orifices of an unanesthetized dog.

bladder, and hemostatic ligatures are applied. The urethra is identified and freed with a curved dissecting scissors from its laterodorsal mesentery on each side and from adjacent fatty tissue; it is mobilized as far distally as possible (Fig. 1) and ligated with 2-0 silk at its distal end.

A hemostatic clamp is applied to the urethra immediately proximal to the ligature and the urethra is divided between clamp and ligature. Care is taken to preserve the branches of the inferior mesenteric and internal pudendal arteries which enter the trigone between ureter and urethra on each side. These vessels, however, may not be essential to the viability of the trigone and the adjacent urethra. Thus, in one animal, all vessels were divided which enter

the bladder, its trigone, and the transected urethra so that the explanted trigone, the adjacent central portion of the bladder and the urethra were attached to the animal solely by the ureters. The trigone and urethra nevertheless remained pink and healthy although supplied exclusively by intramural ureteral vessels.

With a fine-curved intestinal needle, ligatures of 4-0 silk are applied to the vessels which run longitudinally on the surface of the bladder at about 2 cm. from the entrance of the ureters into the bladder (Fig. 1). The abdomen is closed about the mobilized exteriorized bladder without strangulating it or obstructing the urethra. In closing, sutures are not applied to the peritoneum, as they are useless caudal to the semilunar line.

The rectus abdominis muscle is approximated by sutures and the strong anterior rectus sheath is united by closely set ligatures of 3-0 silk; the subcutaneous tissues are apposed by 4-0 silk. The skin is not closed as yet.

Two Allis clamps are applied to the apex of the vesical fundus and the fundus is punctured with a knife between the clamps. The urine is allowed to flow over a towel until the bladder is empty; the towel is then discarded. With a cutting cautery, the bladder is cut through its thickness along the line of the urachus and downward so as to slit the urethra longitudinally along its ventral surface. The clamp on the distal end of the urethra is removed and cautery applied to this end of the urethra to prevent bleeding. The bladder is then trimmed off a few millimeters distal to the line circumscribed by the row of fine ligatures (Fig. 2).

A narrow crescentic strip of skin is trimmed from each margin of the cutaneous incision. The bladder and the mobilized urethra are sewn to the skin by everting mattress sutures alternating with simple sutures, both of 4-0 silk. The ureteral orifices are examined for emission of urine. If the bladder is cyanotic and no urine appears from the ureters, a suture or two should be removed from the rectus sheath to relieve obstruction. The final result is an explantation of the central portion of the bladder, including the trigone and proximal portion of the urethra, to the skin of the ventral abdominal wall. The explant is covered with sterile gauze and dressed with a dry, sterile towel. The dressing is removed after 24 hours. The stitches are removed on the sixth day. Samples of the finished products appear in Figures 5, 6, and 7.

The skin of the inner thighs and the lower abdomen was treated with 70 volumes per cent ethyl alcohol once or twice daily. This tended to prevent cutaneous necrosis and sloughing due to urine. Animals which frequently licked their explant did best in the long run. If a cutaneous cicatrix developed about the exteriorized bladder, thus inverting it, the scar was cut painlessly with a knife.

COLLECTION OF URINE

The urine from each ureter was collected by suction into a 50 cc. round-bottomed centrifuge tube by the equipment shown in Figure 4. This amount

of suction causes inappreciable evaporation of urine from the collecting tubes during diuretic flows. During antidiuretic flows, evaporation is appreciable during collections of 15 or more minutes. The values for renal clearance are not altered by evaporation, however, because, when the volume of urine is reduced by evaporation, the concentration of solutes rises proportionately so that the product of the concentration and the volume remain constant.

The ends of the glass tubing which were applied to the ureteral orifices (Fig. 8) were flared out into conical cups by a torch flame and a cone-shaped piece of carbon.

When catheters, whistle-tip or Braasch-bulb, were inserted into the ureters, urine trickled around the catheter and thus collection could not be complete. This, and the risk of retrograde pyelonephritis, caused abandonment of the method.

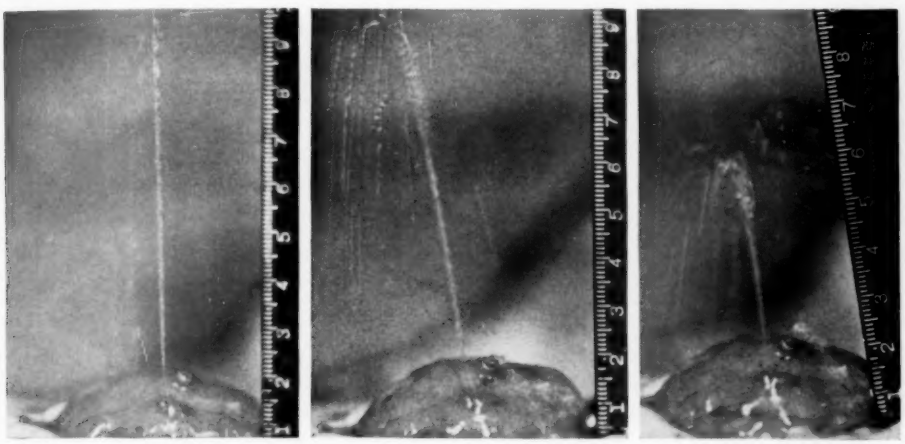


FIG. 9.—Urine spurting from the external orifices during marked diuresis.

The distance between the external ureteral orifices varied considerably and in an unpredictable manner for a given size of mongrel. In animals varying between 8 and 19 Kg. the orifices were from 3 to 14 mm. apart.

DISCUSSION

Renal function in dogs with an exteriorized trigone was measured at intervals for a few months after exteriorization. Pyelonephritis, as indicated by a reduction in effective renal blood-flow, glomerular filtration, and maximal tubular activity developed only in a minority and this probably due to neglect in daily attention to the explant and only irregular forcing of fluids by stomach-tube.

Within 60 to 90 minutes after administration of 50 cc. water per Kg. by stomach-tube, the urine usually spurted from the ureters as a fountain-display (Fig. 9). The spurts from each ureter typically alternated, even when the volume-flow from both kidneys was significantly unequal. The

spurts, however, were not absolutely regular in time or alternation, thus making central control appear unlikely.

BILATERAL CUTANEOUS URETEROSTOMY

Bilateral cutaneous ureterostomy was performed in three animals. The ureters were divided close to the bladder and mobilized for several centimeters. There is an adequate intra-ureteral arterial supply, from the renal and ovarian or spermatic arteries, which assures normal motility in spite of distal mobilization. Spurting vessels at the divided end of the ureter were carefully ligated with fine 4-0 silk. The ureters were brought out through ventrolateral stab wounds, without torsion and under optimal stretch; they were stitched to the skin by 4-0 silk, which was passed through only the ureteral adventitia by a fine-curved intestinal needle. Nevertheless, the exteriorized portions of the ureters tended to become edematous and scarred within a few days and thus to obstruct the normal outflow of urine. In man this is obviated by maintaining a catheter in the ureter until healing is complete; in the dog this was not feasible. This method of collecting urine separately from each kidney was therefore abandoned.

SUMMARY

A method of exteriorizing the canine vesical trigone, with adjacent bladder and urethra, and the manner of collecting urine from each external ureteral orifice are described.

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FACTORS INDUCING RENAL SHUT-DOWN FROM LYSED ERYTHROCYTES: AN EXPERIMENTAL STUDY*

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I. INTRODUCTION

Patients to whom transfusions of blood are given are usually in shock. In acute cases, the arterial pressure is often subnormal and the cardiac output typically diminished. The renal blood flow, in shock, does not remain a constant fraction of the cardiac output but falls actually more than the cardiac output. This is true not only in shock from hemorrhage (Cournand, *et al.*,[12]; Lauson, *et al.*,[27]) and chronic blood loss (Bradley and Bradley[8]) but also when the cardiac output is subnormal in spite of hypervolemia, as may occur in myocardial failure (Merrill[34]; Mokotoff, *et al.*[35]).

Individuals with chronic severe anemia may have a normal arterial pressure, an actually elevated cardiac output, an elevated venous pressure, but a remarkably low blood volume (Sharpey-Schafer[40]; McMichael[29]). Cardiac output, then, is maintained by the rise in venous pressure probably caused by a generalized constriction of capillaries and venules including renal vessels. In short, patients for whom blood transfusion is indicated have a contracted renal vascular bed and a diminished rate of glomerular filtration. A decreased effective renal blood flow in the absence of intrinsic renal damage is probably our most sensitive index of shock, especially of "chronic shock."

Intravenous administration of moderate amounts of hemoglobin or of lysed homologous or autologous red cells to normal man (O'Shaughnessy, *et al.*[36]) and normal dog may not be as nocuous as is generally believed. This suggests that patients who have undergone renal failure from a pint or less of incompatible blood probably had initial renal ischemia from a diminished blood volume.

Thus we set out to find factors which promote renal shut-down from lysed red cells and to locate the mechanism of the shut-down.

II. METHODS

1. *Exteriorization of the vesical trigone* and collection of urine has been described in the preceding paper (Maluf[30]).

2. *Renal Denervation.* The kidney was delivered through a subcostal incision. The perinephric tissue was dissected away until the kidney was attached to the body solely by its artery, vein and ureter. The renal artery and vein were carefully freed from their adventitia, by a fine watchmaker's forceps, for a distance of about 1.5 cm. from the hilum. The ureter was freed from connective tissue for a like distance. The stripped vessels and ureter

* Submitted for publication, October, 1948.

were painted with 50 per cent phenol in ethanol. As soon as the phenol tarnished the vessels it was washed off with alcohol and aqueous zephiran.

To find whether the above method produces effective denervation, one kidney was so treated and the other left intact. A few days later renal clearances were measured simultaneously from each kidney before and after a large intravenous dose of epinephrine hydrochloride (0.22 mg./Kg.). There resulted a marked reduction of effective renal blood flow and glomerular filtration in the denervated but not in the normal kidney (for details see Maluf, 1949[31]). This potentiation to epinephrine has been described by Schneider and Wildbolz[41] and Kubicek and others.[23] Thanks to the exteriorized vesical trigone it was possible, in our work, to use the normal kidney as control for the contralateral denervated organ in the unanesthetized animal.

3. *Renal Function.* (a) *Maximal concentration and dilution.* Water was withdrawn from the cage at about 6 P.M. Next morning the antidiuretic urine was collected in one scoop after it had collected in the groin of the supine animal, hence there could be no increase in concentration by application of prolonged suction. Diuresis was produced by the administration of 50 cc. tepid tap water per Kg. by stomach tube. The specific gravity was measured pyknometrically in a small thin-walled pipette with pointed tip and internal constriction so as to contain from 0.3 to 1.0 cc. of liquid.

(b) *Glomerular filtration, effective renal blood flow and tubular maximum for para-aminohippurate* have been measured as described elsewhere (Maluf, 1949b[31]). All measurements were made on unanesthetized trained animals.

4. *Lysed Erythrocytes.* Blood was collected aseptically from the femoral artery, which was exposed and painted with formalin to kill organisms which may have entered with the cutaneous incision (Pope, *et al.*,[38]). The erythrocytes were allowed to sediment in a refrigerator; if they did not sedimen adequately they were centrifuged. The blood was used within a few days of collection. Within half an hour before infusion, the plasma was aspirated and the cells lysed by adding one and one-half times their volume of apyrogenic distilled water. The hemolysate was transferred through a gauze filter to an Upjohn transfusion bottle containing sodium chloride for isotonicity. The drip was at about 12 cc. per minute into an external jugular vein. If the dog became too dyspneic after about 600 cc. had entered, it was allowed up for a few minutes and then the infusion was completed. At the end of the infusion the hemolysate showed only a trace of methemoglobin spectrophotometrically. Since free hemoglobin in solution steadily changes into methemoglobin (Amberson, *et al.*[2]), the hemolysate was used immediately. Cultures of the hemolysate on blood agar and in enriched broth showed no growth.

5. *Histamine shock* lasting over one and one-half hours was produced by subcutaneous injection of histamine dihydrochloride suspended in cottonseed oil and lanolin (Hueper and Ichniowski[22]).

6. *Intra-aortic Injection with India Ink.* Higgins' India ink was diluted 1:1 with 1.8 per cent sodium chloride. Under nembutal (30 mg./Kg.), a

midline laparotomy was performed carefully and almost bloodlessly. Twenty cc. of the diluted ink were injected in retrograde fashion through a bent needle into the aorta immediately caudal to the renal arteries. The renal pedicles were tightly clamped within half a minute of the injection. Care was taken to avoid pressure on the kidneys and any mobilization of the kidneys until the injection was over and the pedicles clamped. A No. 20 needle was usually used and this caused severe bleeding after its withdrawal unless the aorta was then clamped proximally. When the pedicle clamps were applied too late, as occurred occasionally in the earlier trials on normal dogs, the cortex sometimes stained less than the medulla. This was presumably due to a washing away of ink by the inflow of unstained blood into the cortex on its way to the medulla: a phenomenon noted by Trueta, *et al.*[43] by roentgenography. When digital pressure was applied to a portion of the renal cortex during the injection, that local portion failed to be injected.

III. RESULTS

1. Effects of Intravascularly Injected Lysed Erythrocytes on Renal Function. Four normally hydrated dogs received relatively large doses of freshly lysed canine erythrocytes in isotonic sodium chloride intravenously. The dog in the sample protocol below received about 5.8 Gm. of free hemoglobin per Kg. A dog has 1.2 times as much renal mass per unit of body weight as a man; furthermore, a dog's kidney is about twice as active as a man's per unit of renal weight. Thus, relative to the magnitudes of glomerular filtration and effective renal blood flow, this would be equivalent to giving about 169 Gm. of hemoglobin to a 70-Kg. man $\left(\frac{5.8 \times 70}{1.2 \times 2} = 169\right)$. This is the amount of hemoglobin contained in about 1.4 liters of blood at 12 Gm./100 cc.

These dogs had received 50 cc. of tap water by stomach tube every few days to flush their kidneys and prevent retrograde infection from their exteriorized trigone. Urinary pH during diuresis was between 5.0 and 6.0. Their diet was a mixture of horse meat and cereal. The pH at the exteriorized bladder during antidiuresis was alkaline, doubtless because of the ammonia produced by urea-splitting bacteria.

Measurements of renal function (glomerular filtration, effective renal blood flow, tubular maximum for para-aminohippurate, and maximal concentrating and diluting power of the kidneys) showed practically no change from one day to several days after the infusion.

PROTOCOL

28 July, 1947 Female mongrel; 15.6 Kg. Vesical trigone exteriorized.
18 August Measurements of antidiuretic and diuretic urinary flow and specific gravity (Fig. 1).

29 August — Renal function as follows:

Glomerular filtration	= 40 cc./min. (left kidney).
Glomerular filtration	= 42.6 cc./min. (right kidney).
Effective renal blood flow	= 186 cc./min. (left kidney).
Effective renal blood flow	= 193 cc./min. (right kidney).
Tubular maximum for PAH	= 11.6 mg./min. (left kidney).
Tubular maximum for PAH	= 10.1 mg./min. (right kidney).
Diuretic urinary flows	= 3.34–4.28 cc./min. (left kidney).
Diuretic urinary flows	= 3.14–3.70 cc./min. (right kidney).
pH of urine in diuresis	= 6.0
Hematocrit	= 40.4 vol. %
Blood urea	= 38 mg./100 cc.

8 September — 270 mg. nembutal, s.c., for sedation

Minutes:

0-75 — *1,070 cc. of freshly lysed red cells in isotonic saline through external jugular vein* (= 73.8 cc./Kg. and 5.8 Gm. Hgb./Kg.) The urine was brick-red within 5 minutes after beginning the infusion. Diuresis set in.

No shivering.

80-85 — Rates of urinary flow:
2.18 cc./minutes from left ureter.
2.80 cc./minutes from right ureter.

90-94 — Rates of urinary flow:
2.2 cc./minutes from left ureter.
2.9 cc./minutes from right ureter.
No casts in urine.

94 — Vomits food eaten 3 hours before infusion. (The dogs which were not fed on the day of infusion and which received red cells lysed by apyrogenic distilled water did not vomit or retch on the same day after the infusion; see protocols below).

95 — Walks to cage in good condition.

135 — Vomits more of food eaten before the infusion. Drinks water.

345 — Retches occasionally. Active and alert. Red stream of urine from cage to gutter about 3 meters away; still urinating amply. Water removed from cage. Has drunk 500 cc. water in 165 minutes.

Feces normal in color and consistency; sclerae normal in color. No further vomiting.

Next Morning — About 260 cc. dark-red, thick urine in pan below cage. Hemochromogen still prominent in urine. Holds 800 cc. tap water given by stomach tube to evoke diuresis.

Renal function as follows:

Glomerular filtration	= 37.6 cc./min. (left kidney).
Glomerular filtration	= 42.4 cc./min. (right kidney).
Effective renal blood flow	= 208 cc./min. (left kidney).
Effective renal blood flow	= 222 cc./min. (right kidney).
Tubular maximum for PAH	= 12 mg./min. (left kidney).
Tubular maximum for PAH	= 14.1 mg./min. (right kidney).
Diuretic urinary flows	= 1.61–2.1 cc./min. (left kidney).
Diuretic urinary flows	= 1.7 –2.5 cc./min. (right kidney).
pH of diuretic urine	= 6 to 6.5

No casts in urine

Flow (cc./min.)

Flow (cc./min.)

13 Sept. No water since evening before in preparation for concentration and dilution tests:
Sp. Gr. = 1.004 to 1.047 (left kidney).
Sp. Gr. = 1.002 to 1.053 (right kidney).
Can concentrate and dilute as before the infusion (also Fig. 1).

21 Sept. Both kidneys again show normal concentrating and diluting power. Dog remains healthy.

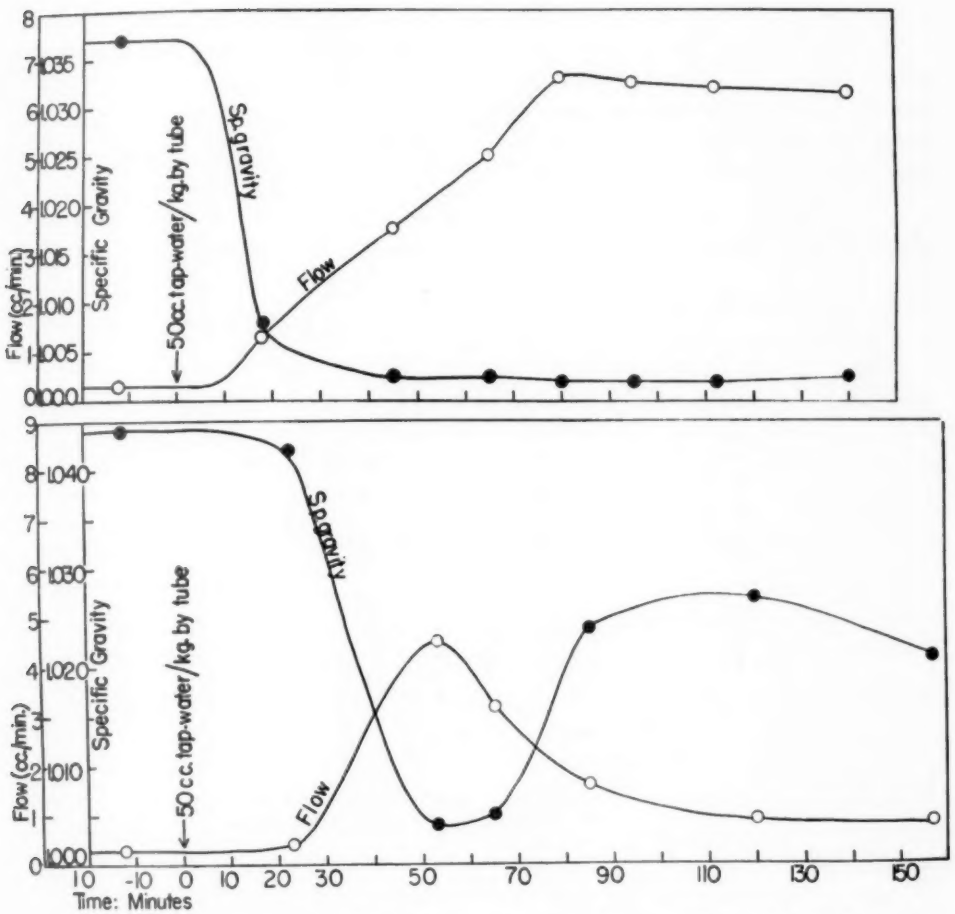

FIG. 1.—Diuretic and antidiuretic urinary flows and specific gravities before and after ingestion of a large quantity of water in a normally hydrated dog before (upper graph) and one day after (lower graph) the infusion of lysed red cells. Free hemoglobin received: 6 Gm./Kg. Maximal and minimal concentrating power is still present after the infusion.

2. Effects of Intravascularly Injected Lysed Erythrocytes Plus Dehydration on Renal Function. There was a marked difference between the effects of intravascularly injected lysed red cells into well hydrated and into severely dehydrated dogs. The former lived without obvious renal injury. The latter became anuric or oliguric and underwent severe renal damage. Below is one

exemplary protocol out of six, all of which had a uniform outcome. To study their renal circulation in the anuric or oliguric phase, the dogs were sacrificed before a probable uremic death.

Dehydration was continued until the urinary flow was 0.006 cc./Kg./min., this being the value found by Harrison and others[20] to foster renal shut-down from 4 Gm. of hemoglobin per Kg. or from 1 Gm. of methemoglobin per Kg.

Any fall in blood volume, which probably occurred during dehydration, was more than fully compensated by the intravenous injection of the hemolysate. The volume infused was about two-thirds of the theoretical normal blood volume and the external jugular veins became engorged. The arterial pressure was always normal, as indicated by the prominently visible femoral pulse. Consequently, the postinfusion renal shut-down could not have been due to hypopiesia.

One dog underwent *renal denervation* about two weeks before receiving the infusion. This conspicuously failed to prevent renal failure.

PROTOCOL

27 Mar. 48	Female mongrel; 12 Kg. Vesical trigone exteriorized.
12 May	Renal function as follows:
	Glomerular filtration = 35.1 cc./min.
	Effective renal blood flow = 226 cc./min.
	Tubular maximum for PAH = 8.1 mg./min.
	Diuretic urinary flow = 1.76–2.88 cc./min.
	NPN. = 57 mg./100 cc.
	Hct. = 32 vol. per cent.
13 May	*Water out of cage in* A.M.*; commencement of dehydration.*
	Weight = 11.8 Kg.
16 May	Refuses food for first time
18 May	Mouth and nostrils parched; temples, cheeks and eyes sunken
A. M.	Urinary flow = 0.005 cc./Kg./min.
	Weight = 10.4 Kg.
	Hct. = 38.9 vol. per cent.
	NPN. = 31 mg./100 cc. plasma
Early P. M.	100 mg. nembutal S.C. for sedation.
Minutes:	
0	*Infusion of lysed red cells in isotonic NaCl begun.*
10	Reddish-brown pigment in urine.
40	Diuresis begins; about 420 cc. of hemolysate in; dog dyspneic, struggles and whimpers; contralateral jugular vein is distended. Infusion discontinued. Dog allowed about.
55	Dyspnea ceases; *infusion recommenced.*
	Mild diuresis continues with dark brown-red pigment.
75	Total amount infused = 555 cc.; = 53.3 cc./Kg. and 2 Gm. Hgb./Kg.
115	Animal drowsy; sleeping in cage; external jugular veins distended; no vomiting.
265	About 50 cc. "black water" in pan below cage. Less drowsy; allowed 50 cc. water by mouth.
325	No vomiting as yet; allowed another 50 cc. water by mouth.
Next morning	No fluid in pan under cage; thighs quite dry.
	Markedly oliguric; less than 0.004 cc. urine per min.; urine dark brown and turbid. Alert but weak.

11: 30–40 A. M. Drank 950 cc. milk.

12:50 P. M. Allowed 300 cc. water, which was soon vomited together with some of the milk drunk two hours ago.

1:20–1:42 P. M. No urine from ureteral orifices, even on dilating orifices.
T = 101.7°F (normal); R = 19/min.
External jugular veins are prominent when lying down but dog still appears strikingly dehydrated and emaciated. Drowsy but readily awakened. Iris tinged red.

2:00 P. M. Weight = 11.3 Kg. NPN. = 156 mg.
Hct. = 39.5 vol. per cent
Hgb. in plasma is almost as intense as in infusion solution.

2:10–2:20 *Still anuric.*

2:25 P. M. Nembutal: 30 mg./Kg. I. V. for anesthesia.
Laparotomy (midline without blood loss): liver not enlarged; viscera grossly normal; stomach distended with about 400 cc. curdled milk and some gas. Gross appearance of kidney normal. 20 cc. of India ink, which had been diluted with an equal volume of 1.8 per cent NaCl, were injected rapidly and in retrograde fashion into the abdominal aorta somewhat caudal to the right renal artery. The renal pedicle was then clamped immediately. The renal cortex was as well injected as the medulla (Fig. 6). The renal capsule was not under tension.

The kidney was fixed in 10 per cent formalin. Frozen sections (8μ and 25μ) were immersed in water to uncurl. Temporary preparations were covered with a droplet of water and a coverslip. The loops of the glomerular tuft were well filled with India ink (Figs. 2 and 3), which was restricted entirely to the blood vessels. There were numerous eosinophilic casts filling practically every collecting tubule in the field (Fig. 4). Elongate, light-brown *crystals*, probably of methemoglobin, were numerous in the tubular lumina (Fig. 5). The tubules were not dilated. There was intracellular pigment and, as shown by H. and E. mounts, no "lower nephron nephrosis."

In another dog, a 16-Kg. pointer which had received 3.2 Gm. of hemoglobin per Kg. as lysed red cells, there was an appreciable urinary flow of 0.187 cc. per minute by the second postinfusion day, this animal never having become anuric. As a gauge of renal function, however, this flow would be misleading since the plasma NPN was 182 mg./100 cc.; there was an almost hundred-fold reduction of glomerular filtration (98 cc. per minute initlally, down to 1.14 cc. per minute on the second postinfusion day), and of *effective* renal blood flow (761 cc. per minute initially, down to 6.4 cc. per minute on the second postinfusion day); and there was a failure to concentrate urine as shown by a low specific gravity and a urine-plasma-creatinine ratio of only 6. These values contrast strikingly with the oliguria of normal kidneys, in which there is maximal concentration during severe dehydration. Thus the urine-plasma-creatinine ratio of dogs subjected to comparable dehydration alone exceeds 200 (see below). Injections of India ink into the abdominal aorta during life showed that, in these dehydrated postinfusion dogs, the *absolute* renal blood flow was ample and the anuria or oliguria could not be explained by renal ischemia. Any hypovolemia which may have

resulted from dehydration was more than fully compensated for by the infusion. The injections were retrograde to avoid the objection that intrarenal vessels may be forced open by the small force of injection. Equal deposition of India-ink particles in blood vessels of the renal cortex and medulla showed that there was no shunting of blood from the cortex. These facts, together with the large number of pigmented and crystalline casts in the tubules and the

FIG. 2 FIG. 3

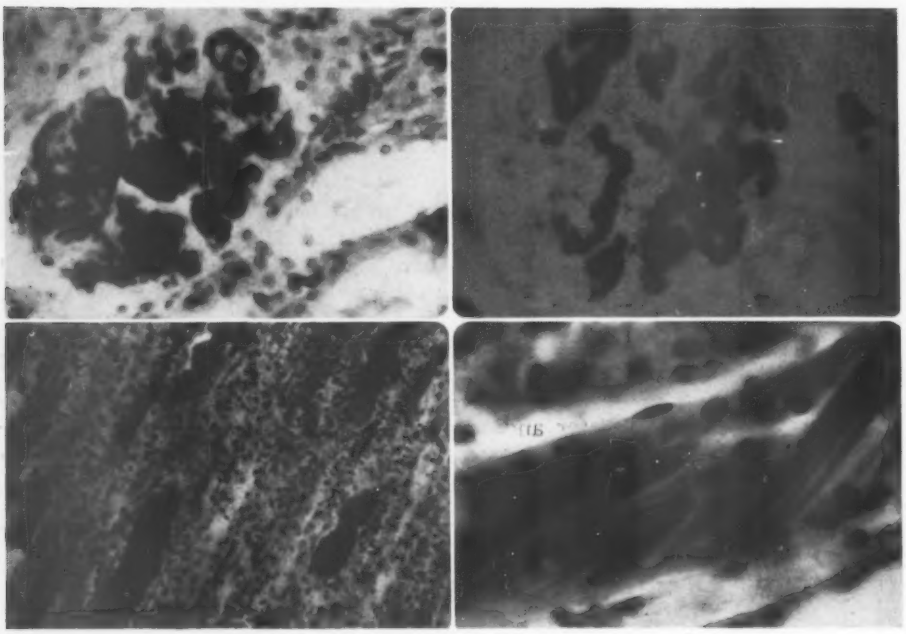

FIG. 4 FIG. 5

FIG. 2.—Glomerular tuft filled with particles of India ink injected during life into the aorta while the animal was anuric from intravenous administration of lysed erythrocytes superimposed on dehydration. Kidney fixed in formalin, section while frozen, and stained with hematoxylin and eosin.

FIG. 3.—Glomerular tuft containing particles of India ink; from same kidney as shown in Figure 2; fresh, frozen preparation; not stained.

FIG. 4.—Pigmented amorphous casts filling collecting tubules of same dog as is seen in Figure 2. Kidney fixed in formalin; sectioned while frozen; stained with hematoxylin and eosin.

FIG. 5.—Elongate crystals, probably of methemoglobin, in the collecting tubules of the same dog as is seen in Figure 2. Same preparation as in Figure 4.

absence of histologic evidence of renal cellular damage, indicate that the anuria or oliguria are, initially, at least, caused by tubular obstruction. The fact that the animals were not allowed to progress and die in uremia may explain the absence of increased intracapsular tension, absence of histologically obvious renal cellular damage and absence of peritubular edema.

3. Effects of Dehydration Alone on Renal Function. It was essential to study the effects of dehydration alone on renal function. The following protocol

shows that severe dehydration alone actually can reduce, reversibly, glomerular filtration and effective renal blood flow by about half. The specific gravity of the urine, however, becomes high. This contrasts with the low fixed specific gravity in oliguria from intravascular administration of lysed red cells plus dehydration. Parallel with the high specific gravity is the high urine-plasma ratio for creatinine, which contrasts with a low ratio in oliguria from dehydration combined with intravascularly given lysed red cells (see protocol). The renal shut-down in the latter dogs is accurately depicted not so much by the oliguria *per se* as by the great fall in glomerular filtration and effective renal blood flow. Unilateral renal denervation in a dog, the protocol of which is not presented here, did not alter the extent of reduction in renal function by dehydration alone.

PROTOCOL

28 November, 1947 Female mongrel. 9.3 Kg.
Exteriorization of vesical trigone. NPN = 32 mg./100 cc.

28 May, 1948 Renal function as follows:
Glomerular filtration = 58.9 cc./min.
Effective renal blood flow = 438 cc./min.
Diuretic urinary flow = 3.2–3.89 cc./min.
Urine-plasma ratio for creatinine = 18.4
Hct. = 49.2 vol. per cent.

9 June *Water out of cage; commencement of dehydration.*

14 June Rejects food for first time.

16 June Weight = 7.9 Kg. NPN = 36 mg./100 cc.
Urinary flow = 0.0061 cc./Kg./min.
Sp. Gr. = 1.042.
Renal function as follows:
Glomerular filtration = 23.5 cc./min.
Effective renal blood flow = 187 cc./min.
Urinary flow = 0.10 cc./min.
Urine-plasma ratio for creatinine = 235.0
Hct. = 54.3 vol. per cent
Shortly after the above measurements the dog was allowed to drink water as desired (= about 1,000 cc.), a large part of which was promptly ejected. Alert and active.
No further vomiting. One and one-half hours later it ate 1 pound of canned canine food. Six hours later it ate another pound.

19 June Weight 9.2 Kg. Hct. = 49.2 vol. per cent.
Renal function as follows:
Glomerular filtration rate = 45.2 cc./min.
Effective renal blood flow = 270 cc./min.
Diuretic urinary flow = 1.8 cc./min.

4. Effect of Intravascularly Injected Lysed Erythrocytes Plus Shock on Renal Function. It was important to find whether renal shut-down would result from the injection of lysed red cells into normally hydrated dogs if shock were superimposed.

Reversible shock was produced by injecting histamine dihydrochloride in oil subcutaneously into normally hydrated dogs. The infusion of lysed red

cells was performed when the dog was in prostrate shock. Even though the volume of solution infused was almost as great as the theoretical circulating blood volume, the effect of the infusion on the shock picture was not striking. The anuria of shock changed only to a scant urinary flow during the infusion. A few hours later, even after complete recovery from shock, there was absolute anuria or marked oliguria.

The oliguria caused by intravascularly injected lysed red cells plus shock is a genuine renal shut-down with at least a hundred-fold decrease in glomerular filtration and effective renal blood flow, a low urinary specific gravity, a

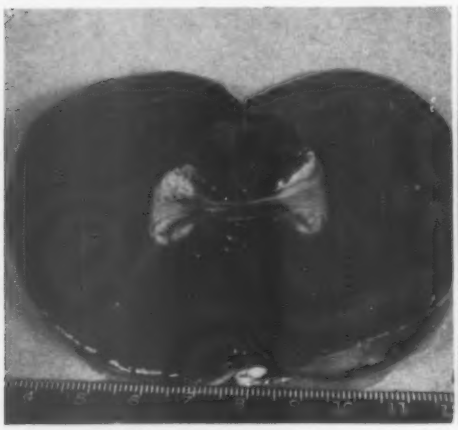

FIG. 6

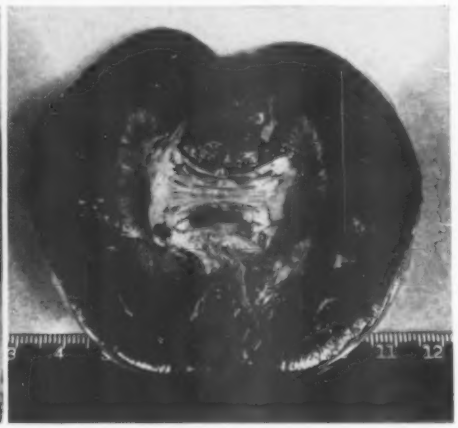

FIG. 7

FIG. 6.—Divided kidney of the dog which was sacrificed in anuria from intravenous administration of lysed red cells superimposed on dehydration (same dog as in Figs. 2 to 5). India ink was injected during life into the aorta and the renal pedicle was clamped immediately after. Both the cortex and the medulla are well injected.

FIG. 7.—Divided kidney of the dog which was sacrificed in anuria from intravenous administration of lysed red cells superimposed on histamine shock. The arterial pressure was normal at this time. Intra-aortic injection of India ink with immediate subsequent clamping of the renal pedicle resulted in equal and normal injection of both cortex and medulla.

low urine-plasma ratio for creatinine, and a marked uremia. This type of oliguria is identical with that from lysed red cells plus severe dehydration, and contrasts with the oliguria of severe dehydration alone (see above).

Injections with India ink, as described above, during the phase of *post-shock* renal shut-down, resulted in equal and adequate injection of the renal cortex and medulla. This indicates a normal absolute renal blood flow and shows that the renal shut-down cannot be due to a shunting of blood from the renal cortex to the medulla. The casts in the tubular lumina indicate extensive tubular obstruction as the primary cause of the shut-down. Here again the marked fall in effective renal blood flow, as measured by the para-aminohippurate clearance, is obviously due to inability of the tubules to allow passage of the hippurate because of their being obstructed.

Animals which were put into shock with the above dose of histamine, but which did not receive lysed red cells, recovered completely although they were

anuric for more than an hour. India ink injections during the anuria from shock showed merely a diminished injection of the kidneys with more ink in the renal cortex than in the medulla. Thus the anuria during histamine shock is the result of general renal ischemia and not the outcome of a shunting of blood from the renal cortex to the medulla.

The experiment of injecting lysed red cells into normally hydrated dogs in shock was done on three animals.

PROTOCOL

	Female mongrel; 13 Kg. Vesical trigone had been exteriorized.
6 June, 1948	Renal function as follows:
	Glomerular filtration = 50 cc./min.
	Effective renal blood flow = 290 cc./min.
7 June	Weight = 13.0 Kg. Food and water withdrawn from cage at 6 P. M.
8 June	Urinary flow = 0.16 cc./min.
	Sp. Gr. of urine = 1.041
	pH of urine = 6.0
Minutes:	
0	Femoral arterial pulse strikingly visible through skin; exteriorized bladder pink; R = 20/min.
	70 mg. histamine dihydrochloride (= 5 mg./Kg.) in 3 cc. cottonseed oil plus lanolin, s.c. through a No. 18 needle; tape was applied over the site.
23	Lies prone.
33	Stands and ejects bile-stained vomitus.
58	Around and walking; defecates.
68	Lying down with eyes half closed; femoral arterial pulse no longer visible but thready to palpation.
77–82	Urinary output not measurable; 1 drop; bladder a mottled purple-red. Dog markedly drowsy.
	Blood draw now showed: Hct. = 43.7 vol. per cent; NPN = 29 mg./100 cc.
78	*Infusion of lysed canine red cells in isotonic NaCl begun.*
78–133	No shivering; 1 to 2 drops of urine; normal in color.
134	Urine appears; not a copious flow; dark brown in color.
153	*Infusion discontinued.* Volume infused = 650 cc. (= 50 cc./Kg. and 3.76 Gm. Hgb./Kg.).
158	No diuresis; urinary flow still scant; dog licks lips; drowsy; lies prone.
163	Blood sample drawn now shows: Hct. = 41.7 vol. per cent; Plasma Hgb. = 2.8 Gm./100 cc.
168–173	Dark-brown urine; less than 0.02 cc./min.
273	Urinary flow still less than at 168–173 min.
	Femoral arterial pulse still not visible but feels more forcible; dog can stand but prefers to lie down. Bladder no longer markedly cyanotic. T = 101°.6F.
296	Vomits.
396–404	Femoral arterial pulse now distinctly visible although not as prominent as initially.
	Urinary flow less than 0.01 cc./min.; urine dark brown.
	Jaundice apparent on exposed areas of skin, such as inner portions of earflaps and belly.
660	Anuric. Alert and active. Ate almost 1 pound canned canine food; refused the rest. Allowed about 200 cc. water.

Next morning — Urinary flow = 0.01 cc./min., urine dark brown; jaundice increased; no "black water" in pan under cage during night but about 300 cc. of what looks like chiefly vomitus. Dog moderately alert and active.
Blood showed:
NPN. = 1122 mg./100 cc.
Hct. = 40.3 vol. per cent
Plasma Hgb. = 2 Gm./100 cc.
Drank, as desired, 140 cc. water, which was vomited after 20 minutes.

Evening — Is listless; retches when offered food.

Second postinfusion day — Listless but can walk. T = 99.°8F. Urinary flow is less than 0.006 cc./min.; urine a light brown; stools not tarry; no hyperpnea.

Third postinfusion day — Weight = 11.7 Kg. T = 98°6F. R = 48.
Femoral arterial pulsations visible; alert but listless; neuromuscular hyperirritability; Chvostek. Practically no fluid in pan at bottom of cage; a small, loose, deep-brown stool; urine a dark orange. Bleeding time elevated.
Urinary flow = 0.079 cc./min.
Sp. Gr. of urine = 1.020; Hct. = 47.3 vol. per cent
NPN. = 312 mg./100 cc.
Plasma Hgb. still appreciable (less than 1 Gm./100 cc.); plasma stained with bile pigment
Renal function:
Glomerular filtration = 0.40 cc./min.
Effective renal blood flow = 1.28 cc./min.
Urine-plasma ratio for creatinine = 5.1
Laparotomy under nembutal anesthesia: Subcutaneous tissues and viscera jaundiced; gastro-intestinal tract empty; renal capsule incised in situ and found not to be under tension; extensive oozing of blood from renal cortex when this was nicked slightly. Kidney excised; deeply stained with brown pigment; pigment in medulla darker than in cortex. When the kidney was divided and squeezed gently, more blood seemed to ooze from the cortex than from the medulla. There was thus no evidence of renal cortical ischemia. Intra-aortic India ink showed equal and normal injection of cortex and medulla (Fig. 7).

5. Effects of Intravascular Hemolysis by Distilled Water on Renal Function. Large amounts of apyrogenic distilled water were injected rapidly intravenously into normal hydrated dogs. Only mild, transient systemic effects resulted. The four dogs so treated received an average of 90 cc. of distilled water per Kg. in 18 minutes, which, relative to renal activity (see above), is equivalent to injecting 2,600 cc. into a 70-Kg. man. Renal function, as indicated by concentration and dilution tests and by the plasma—NPN, was not reduced. Landsteiner & Finch[26] injected 200 cc. of distilled water in from one to two minutes into patients who were not in shock and found no rise in blood urea. Voris[44] gave 1,000 cc. of distilled water intravenously to patients and noted no ill effects and only mild hemoglobinuria.

PROTOCOL

Female mongrel; 11.6 Kg.; vesical trigone had been exteriorized; normally hydrated; no food since night before. Initial NPN = 54 mg./100 cc.

14 March, 1948	Left renal artery and vein divided.
17 March	Evaluation of renal function:
	Glomerular filtration = 33.7 cc./min.
	Effective renal blood flow = 174 cc./min.
	Tubular maximum for para-aminohippurate = 13.5 mg./min.
	Diuretic urinary flows = 1.46–2.86 cc./min.
10 June	
2:20–2:38 P. M.	*1,025 cc. apyrogenic distilled water were injected* through a three-way metal cock and No. 15 needle *into an external jugular vein* using a 20-cc. syringe; *i.e.*, 88.5 cc. water/Kg. in 18 min. The exteriorized trigone showed no immediate diuresis or obvious pigmentation of the urine. The dog was not manifestly uncomfortable. It lay down comfortably, shook itself occasionally and belched gas.
	Hct.-before I. V. = 35.7 vol. per cent
	Hct.-after I. V. = 34.6 vol. per cent
	Plasma hemoglobin immediately after I. V. = 200 mg./100 cc.
3:19–3:24 P. M.	Marked diuresis. 4.4 cc./minute of light reddish-brown urine. Dog returned to cage in good condition. Extensive diuresis continues.
5:30 P. M.	Ate 1 pound canned canine food
12 June	NPN = 41 mg./100 cc. Plasma normal in color. Dog concentrates and dilutes urine normally.

6. Effects of Intravascular Hemolysis by Distilled Water Plus Shock on Renal Function. Human beings who are not in shock have been shown to tolerate, without renal damage, rapid intravenous injection of at least 900 cc. of distilled water. It has been suggested that the renal shut-down and uremia which may follow irrigation of the bladder with tap water during transurethral operations on the prostate gland may be due to a combination of shock with intravascular hemolysis (Creevy & Webb,[4] Landsteiner and Finch,[26] McLaughlin, and others[28]). It has not been possible, however, to produce renal failure in dogs by a combination of shock plus injection of distilled water even in quantities which one might not venture in man.

The dog of the following protocol had only one kidney; underwent 90 minutes of absolute anuria from severe shock lasting two hours; was rapidly infused with 95 cc./Kg. of distilled water during the anuria; and did not recover from anuria until 70 minutes after the infusion. This combination of apparently near-maximal adverse circumstances nevertheless failed to produce renal failure. Similar results occurred in the two other dogs so tested. It is possible that overhydration and reversible shock without blood loss prevented uremia. Creevy (1947) has pointed out that aggravating factors in man may be renal vasoconstriction from rapid blood loss, arteriosclerosis and pyelonephritis. This deserves further investigation.

PROTOCOL

	Female mongrel; weight = 8.85 Kg.; vesical trigone had been exteriorized.
7 May	Right nephrectomy.
18 May	Renal function as follows:
	Glomerular filtration = 48.9 cc./min.

	Effective renal blood flow = 250 cc./min.
	Tubular maximum for para-aminohippurate = 17.2 mg./min.
18 June	No food or water since evening before.
Minutes:	
0	Femoral arterial pulse visible through skin; exteriorized bladder pink; R = 22 min.
	5 mg. histamine dihydrochloride per Kg. in cottonseed oil and lanolin, s.c. over chest.
7	Dog lies prone and licks lips.
12	Gets up and defecates.
22	Again lies prone.
42	Retches.
63	R = 40/min. Femoral arterial pulse no longer visible and faint to palpation; exteriorized bladder cyanotic.
63 to 70	*Anuric.*
74 to 90	*850 cc. apyrogenic dist. water I. V., i.e.,* 95 cc./Kg. in 16 minutes. Vomits once during procedure. Defecates.
	Still anuric.
93	Uncomfortable; abdomen distended and rather tympanitic; grunts; stands voluntarily but unsteadily.
95	Blood drawn now shows: NPN = 31 mg./100 cc.: Hct. = 40.3 vol. per cent; Plasma Hgb. = 300 mg./100 cc.
	Dog stands but with head lowered.
125	*Dog still anuric;* lying down.
160	Urinary flow sets in; brownish-red urine; dog *has had about 90 minutes of absolute anuria.* Femoral pulse now forcible to palpation but still not visible through skin; dog lying down; no diuresis as yet.
520	Only 300 cc. of brownish fluid in pan at bottom of cage; urine a light reddish-brown; is distinctly lighter than six hours ago. Dog obviously recovered from shock but refuses food or water.
Next morning	Weight = 8.2 Kg. 750 cc. dark brown liquid in pan at bottom of cage. Urine is light reddish-brown.
	Hct. = 44.2 vol. per cent
	NPN. = 39 mg./100 cc.
	Urinary flow = 0.55 cc./min.
	Plasma hemoglobin somewhat below yesterday. Eats ¼ pound of canned canine food.
Second postinfusion day	Urine straw-colored and output copious; appetite normal. Food and water out of cage at 5 P. M. for concentration and dilution test tomorrow.
Third postinfusion day	Weight = 7.8 Kg.; Hct. = 47 vol. per cent; NPN = 31 mg./100 cc.
	Sp. Gr. of concentrated urine (at 0.16 cc./min.) = 1.029.
	Sp. Gr. of dilute urine (at 2.4 cc./min.) = 1.004.

IV. DISCUSSION

We have shown that normally hydrated dogs may withstand intravenous injection of lysed canine red cells which, so far as relative degrees of renal activity are considered, would be equivalent to the infusion of more than a liter of incompatible blood into a 70-Kg. man. This tolerance is true in spite of aciduria. Earlier studies which indicated a greater tolerance to hemoglobinemia in alkalinuria (Baker and Dodds,[3] for rabbits; De Gowin *et al.*,[15] for dogs) were inadequately controlled especially as to dehydration. Thus, De

Gowin and others made their dogs acidotic by mixing 8 Gm. of ammonium chloride with one-half pound of beef per day. The dogs occasionally refused this food "for several days at a time." Furthermore, while 7 of the 28 dogs died of renal failure, 6 died of intercurrent infection. As for rabbits, Yorke and Nauss[46] have noted the importance of dehydration in posthemoglobinemic anuria. Anuria and death occurred in the rabbits fed dry diets but not in those eating green food. They postulated a low glomerular filtration pressure due to dehydration. De Navasquez[16] and Yuile and others[47] failed to reproduce the results of Baker and Dodds in rabbits. Flink[17] injected from four to six Gm. of hemoglobin per Kg. into dogs and found just as severe renal damage in dogs with alkalinuria as in those with aciduria. When the initial concentration of hemoglobin in the plasma exceeded 3.7 Gm./100 cc., renal insufficiency always developed. He found no difference between the effects of solutions of hemoglobin crystals and of lysed red cells. Bing[6, 7] found from 0.5 to 1 Gm. of hemoglobin per Kg. practically innocuous to dogs, whether in aciduria or alkalinuria, and that methemoglobin was relatively nocuous in aciduric but not in alkalinuric dogs. Bing's anuric dogs, however, may have been dehydrated as a result of large ammonium chloride feedings. Furthermore, ammonium chloride itself, even in doses considerably smaller than Bing's, is somewhat nephrotoxic to man (Markert[32]), and especially to rabbits (Govan and Parkes[19]). Webster and others (1935) have pointed out that in the presence of physiologic salt concentrations, the state of aggregation of hemoglobin is not influenced by pH.

O'Shaughnessy and others[36] injected intravenously into a patient with cancer 50 Gm. of human hemoglobin in 30 minutes. This is equivalent, at least in terms of hemoglobin, to over 300 cc. of incompatible blood. No obvious renal damage resulted. Gilligan and others[18] and Ottenberg and Fox[37] obtained similar results with smaller quantities of hemoglobin; however, Gilligan and others noted chills, fever and severe abdominal pains in the patient receiving the largest quantity of stroma-free human hemoglobin, 16.4 Gm., *i.e.*, only 0.25 Gm. per Kg.

The importance of dehydration in causing renal shut-down from homologous hemoglobin has been shown by Yorke and Nauss[46] and Lalich[24, 25] for rabbits and by Harrison and others[20] for dogs. The present work in part confirms their findings. We have further found that severe dehydration will reduce the effective renal blood flow and rate of glomerular filtration in the dog. This may be true in man, as is indicated by the falling urea clearance and the rising NPN in man's blood during progressive dehydration (Adolph and others.[1]).

That shock plus hemoglobinemia or myoglobinemia can result in renal failure has been shown by Corcoran and Page[10] (1945). The present study in part confirms this.

The cause of renal shut-down from hemoglobinemia has been hypothesized on the basis of renal vasoconstriction, mechanical tubular blockage or

renal tubular damage. Evidence for renal vasoconstriction by free hemoglobin in the blood stream was produced by Reid[39] and Mason and Mann.[33] Hesse and Filatov[21] (1933) found a fall in arterial pressure and renal volume upon infusion of lysed autologous blood into dogs. Subsequent workers, who have performed the infusions aseptically, have not been able to confirm these findings (Bing,[7] 1944; Flink,[17] 1945; Corcoran and Page,[11] 1947). The diuresis which directly follows an infusion of hemoglobin solution into a normal dog and which tends to occur even in a dehydrated or hypopiesic dog contraindicates vasoconstriction as a primary factor in the renal shut-down.

Our studies with India ink indicate no obvious decrease in *absolute* renal blood flow during the anuria or oliguria which follows infusion of lysed red cells superimposed on reversible shock or dehydration. Our measurements of the renal clearance of para-aminohippurate, however, show a very marked fall in *effective* renal blood flow. These findings imply that damaged or obstructed tubules fail to extract the hippurate from the blood circulating through the renal parenchyma. It is significant that these were postinfusion studies and that the animals had recovered completely from shock or had their blood volume fully replenished from any loss incurred during dehydration. They nevertheless had marked renal shut-down. These India-ink studies also show that this renal failure cannot be ascribed to a shunting of blood from the renal cortex to the medulla. Such a shunt has been described by Trueta and others[42, 43] in a certain percentage of rabbits upon stimulation of the sciatic nerve or after injection of staphylococcal toxin.

Renal failure occurred when intravascular injection of lysed red cells was combined with dehydration or shock even in kidneys which had been denervated.

Corcoran and Page[9] incidentally noted that dogs in hemorrhagic shock with denervated kidneys responded to blood transfusion by a disproportionately slow and incomplete return toward normal of renal clearances. They therefore suggested that spinal anesthesia may actually interfere with the recovery of renal circulation in shock treated by transfusion.

Our dogs were sacrificed after a postinfusion period of from two to three days, when they were quite uremic. At this stage, the renal capsule was not under tension and there was no histologically obvious renal cellular damage. Many of the tubules in a field were occluded by brown casts or crystals. The casts were best preserved by fixing the kidney in 10 per cent formalin shortly after the animals were sacrificed and sectioned while frozen a few days later. Most of the casts were lost when the kidneys were sectioned while frozen without prior fixation. The loss probably occurred when the frozen sections were immersed in water to unroll. Although there was considerable loss of casts in specimens carried through paraffin in Flink's[17] studies, the majority of tubules were occluded by casts in dogs with serious or fatal renal damage. This has been confirmed by Lalich[24] and Harrison and others.[20] Harrison and others teased out casts by microdissection and found that they dissolved rapidly in buffers below pH 5.2 and above pH 7.6 and that they had the

spectral properties of methemoglobin. The studies of several investigators, including Bell,[5] indicate that tubular obstruction by pigmented casts is a prominent feature in the renal shut-down of the "transfusion-kidney." By showing the nontenability of the postulate that lysed red cells produce renal cortical ischemia, by studying the kidneys histologically within the first two days after infusion, and by showing that dehydration and shock are predisposing factors, we are left, as our apparent sole gross explanation, the following: *The mechanism of renal failure from the intravascular introduction of a moderate quantity of lysed red cells is primarily due to tubular obstruction from casts of hemochromogen combined with a low rate of glomerular filtration.*

V. SUMMARY

1. As much as 5.8 Gm. per Kg. of free homologous hemoglobin, as lysed red cells, may be given intravenously to a normal, well-hydrated dog without producing any striking sign of renal damage. In terms of lysed red cells and relative to the degree of renal activity, this is equivalent to giving at least one liter of incompatible blood to a 70-Kg. man. The initial urinary pH of the dogs was from 5.5 to 6.0.

2. When a dog is dehydrated until its urinary flow is only 0.006 cc./Kg./min., intravenous infusion of from 2 to 3 Gm. per Kg. of free hemoglobin as lysed red cells will lead to immediate anuria or oliguria and then severe uremia. The resultant oliguria is not of a concentrated but of a dilute urine. A nearly normal urinary output may mask a severe renal shut-down, as indicated by a hundred-fold decrease in the rate of glomerular filtration and *effective* renal blood flow.

3. The oliguria of severe dehydration alone, on the other hand, is of a urine with high specific gravity. Severe dehydration of the above extent results in an approximate halving of glomerular filtration and effective renal blood flow. This is reversible on rehydration and the animal promptly recovers.

4. Denervation of a kidney several days prior to dehydration does not influence the changes mentioned in 2 and 3.

5. Intravenous injection of from 3 to 4 Gm. per Kg. of free hemoglobin as lysed red cells into a dog in profound reversible shock and anuria from histamine will lead to postshock anuria or oliguria and then to severe uremia. As in the combination of dehydration with intravascular injection of lysed red cells, there results an immense fall in glomerular filtration and *effective* renal blood flow and a low urine-plasma ratio for creatinine.

6. Intra-aortic India-ink injections during life show that there is normal intraglomerular and peritubular circulation during the anuria or oliguria of the renal shut-down which follows intravenous injection of lysed red cells during dehydration or shock. There is no shunting of renal blood flow from the renal cortex. The tubules are filled with pigmented amorphous and crystalline casts.

7. The renal capsule is not under tension and there is no histologic evidence of renal cellular damage during the first two or three days of uremia.

8. A dog can stand rapid intravenous injection of 100 cc. of distilled water per Kg. without striking reduction in renal function and with complete recovery. Relative to the degree of renal activity, this is equivalent to rapid injection of 2.6 liters into a 70-Kg. man.

9. A dog can stand rapid intravenous injection of at least 95 cc. of distilled water per Kg., even during profound histamine-shock with its resulting anuria, without undergoing marked reduction in renal function and with complete recovery.

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THE EFFECTS OF ULTRAVIOLET RADIATION ON THE EXPOSED BRAIN—EXPERIMENTAL STUDY*

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THE USE of ultraviolet radiation in the operating room was introduced by Hart[1] in 1936, thereby adding another effective measure for the control of postoperative wound infection. Hart and his associates[2, 8] demonstrated in subsequent publications that air-borne pathogenic organisms were responsible for the majority of infections in clean operative cases and that such organisms could be largely eliminated by ultraviolet radiation. Experimental studies to determine the effect upon wound healing of this physical agent, as well as those concerned with its bactericidal effects, were carried out by this group before recommending its use in the operating room.

A brief account of the reaction of the brain to ultraviolet radiation was given by Hart and Sanger[7] and additional unpublished data derived from animal studies have permitted its use in our neurosurgical operative rooms during the past ten years. In this publication we shall describe the pathological alterations which occur in the cerebral cortex upon exposure to ultraviolet radiation as compared to those which occur upon exposure to atmospheric air alone.

METHOD

Twenty-five dogs were used during the experiment and all operations were carried out under aseptic technic. Intraperitoneal anesthesia was employed, using nembutal one grain per five pounds of body weight. An incision was made in the scalp and the temporal muscle was reflected laterally. A small trephine opening was then placed in the skull and the opening enlarged with rongeurs to a diameter of approximately 3 cms. by 2.5 cms. The dura was opened in an elliptical fashion and reflected laterally, exposing an area of the cortex 2.5 cms. by 2 cms. Twelve of the dogs were exposed to ultraviolet radiation (at an intensity of 16 microwatts per square centimeter)‡ for various intervals from 15 minutes to 3 hours. In a second group of 12 dogs the brain was exposed to air for the same periods of time. One animal was anesthetized for three hours as a control experiment and sacrificed on the

* Submitted for publication, February, 1949.

† We are indebted to the Lamp Division of the Westinghouse Electric Manufacturing Company for supplying the irradiation units used in this study. Dr. D. G. Sharp is responsible for arranging this unit and measuring the intensities used.

‡ This intensity was selected due to the fact that it was the same as the present reading in the neurosurgical operation room.

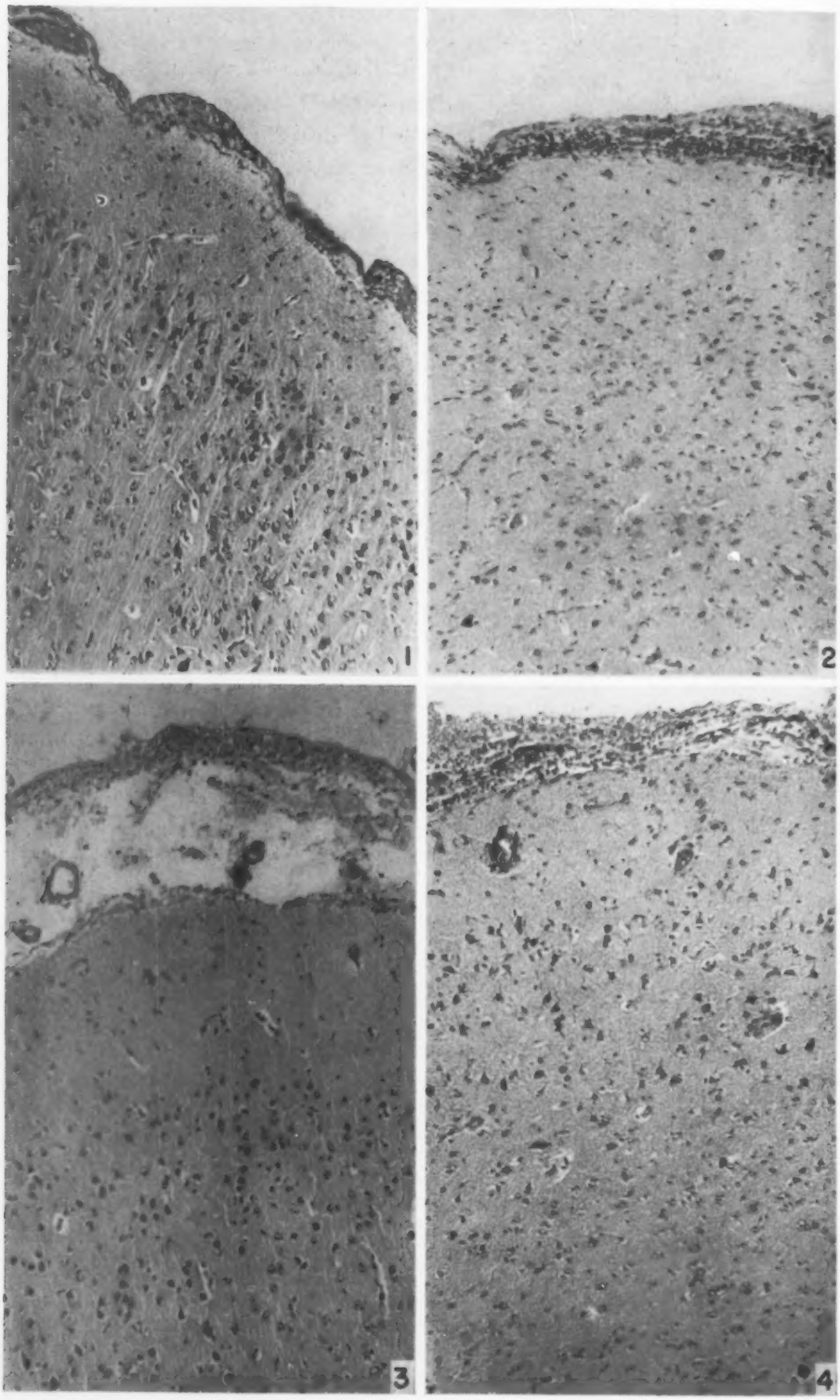
seventh post-anesthetic day, without exposure of the cortex to air or ultraviolet radiation. During the entire exposure of the cortex to air or ultraviolet radiation and air, it was kept moist with Ringer's solution. The dura was closed with interrupted black silk. The muscles and scalp were sutured with interrupted black silk and a sterile gauze collodion dressing applied. The animals were sacrificed by bleeding while under nembutal anesthesia on the third, seventh and twenty-eighth day. The carotid arteries were injected with 10 per cent formaldehyde. Blocks were taken through the exposed area and from the opposite hemisphere and fixed in 10 per cent formaldehyde U.S.P. and ammonium bromide solution of formaldehyde. Sections were stained with hematoxin phloxine, toluidine blue, gold chloride and silver carbonate.

RESULTS

The changes which were observed were progressively dependent upon the length of time of the exposure. After exposure to ultraviolet radiation for 10 minutes the meningeal vessels began to dilate and gradually the brain became congested. Changes in the meningeal vessels in the group exposed to air alone were not apparent until approximately 45 minutes after the exposure had commenced and were never as prominent as those exposed to ultraviolet radiation. Swelling of the brain as noted by bulging of the exposed area was present in the 2-hour and 3-hour radiation groups but was never sufficient to prevent closure of the dura. The swelling was not noted in the one-half or one-hour exposure to ultraviolet radiation. None of the exposures to air, except the 3-hour ones, produced any degree of bulging of the cortex.

Microscopic sections from the specimens exposed to air for 15 or 30 minutes (Fig. 1) or to ultraviolet radiation for 15 minutes showed very little change. The first definite changes which were detected were in those animals exposed to ultraviolet radiation for 30 minutes (Fig. 2). These animals revealed slight thickening of the arachnoid with dilatation of the meningeal vessels and a moderate number of red and white blood cells in the subarachnoid space. There was dilatation of the subpial vessels and widening of the perivascular spaces of the gray matter. These changes became more pronounced in the 1-hour (Fig. 4), 1½-hour, 2-hour and 3-hour specimens (Fig. 5), with white blood cells becoming rather numerous in the subarachnoid space in the exposures of one hour. Subpial hemorrhages were present in the 3-hour exposures to ultraviolet radiation with small perivascular hemorrhages (diapedesis) throughout the gray matter. In one of these animals there was fairly extensive destruction of a triangular area of the cortex by hemorrhage. The brains that were exposed to air for one hour (Fig. 3) or longer showed red blood cells in the subarachnoid space, slight thickening of the arachnoid and an increase in the size of the perivascular spaces but the changes were only slight as compared to those exposed to ultraviolet radiation. In none exposed to air were hemorrhages noted.

The neurons after exposure to ultraviolet radiation for 30 minutes (Fig. 6) began to show definite changes, mainly shrinkage and acute swelling which



FIGS. 1–4.—(Legends on opposite page)

became more marked as the exposure time was prolonged. The neurons which showed shrinkage were located for the most part in the superficial layers of the cortex. These cells were deeply stained, shrunken and triangular. The nucleus and nucleolus could be recognized as such except in the longer exposures when the cell body was markedly shrunken and the nucleus and nucleolus could not be identified. The perineuronal space about these cells was widened. The cells which revealed acute swelling or chromatolysis were more prominent than those which showed shrinkage, and were confined to the deeper layers of the cortex. The cytoplasm of these cells contained vacuoles, and the nucleus was enlarged and displaced to one side of the cell, or occupied the entire cell body. In some instances the contour of the cell was lost, as though the cell membrane had ruptured and all that remained was the swollen nucleolus, fragments of the cell outline or a clear space. These neuronal changes were very pronounced in the 3-hour exposures to ultraviolet radiation and the gray matter presented a honeycombed appearance with a loss of the normal lamination. Minor changes of the same type were present in the exposures to air and such changes began to appear at approximately one hour.

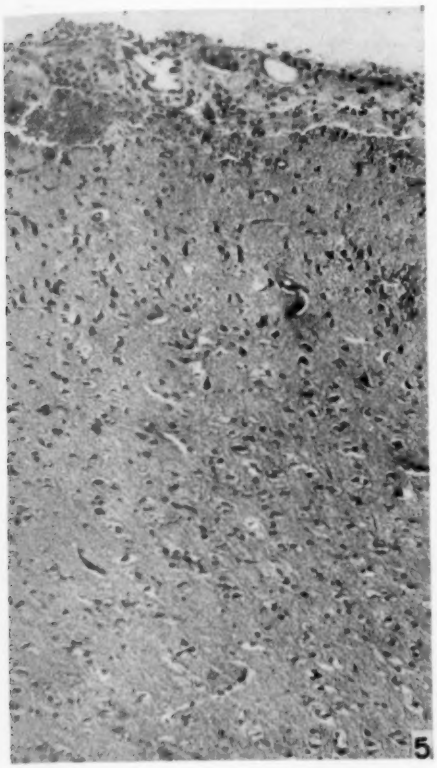


FIG. 5.—Exposure to ultraviolet radiation 3 hours, sacrificed on the seventh day. (Hematoxin phloxine 110 x)

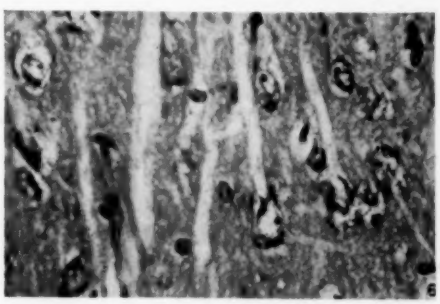


FIG. 6.—Exposure to ultraviolet radiation 30 minutes, sacrificed on the seventh day. (Toluidine blue 580 x)

FIG. 1.—Exposure to air for 30 minutes, sacrificed on the seventh day. (Hematoxin phloxine 120 x)

FIG. 2.—Exposure to ultraviolet radiation 30 minutes, sacrificed on the seventh day. (Hematoxin phloxine 120 x)

FIG. 3.—Exposure to air 1 hour, sacrificed on the seventh day. (Hematoxin phloxine 120 x)

FIG. 4.—Exposure to ultraviolet radiation 1 hour, sacrificed on the seventh day. (Hematoxin phloxine 120 x)

The astrocytes became increased in size and number. This hyperplasia of the astrocytes first occurred in the 30 minute (Fig. 8) exposure to ultraviolet radiation and progressed with the time of the exposure. This change first occurred in the marginal layer but progressed to involve the gray and white matter in the longer exposures. The brain of the dogs exposed to air for 1½ hours began to show a hyperplasia of the astrocytes in the marginal layer.

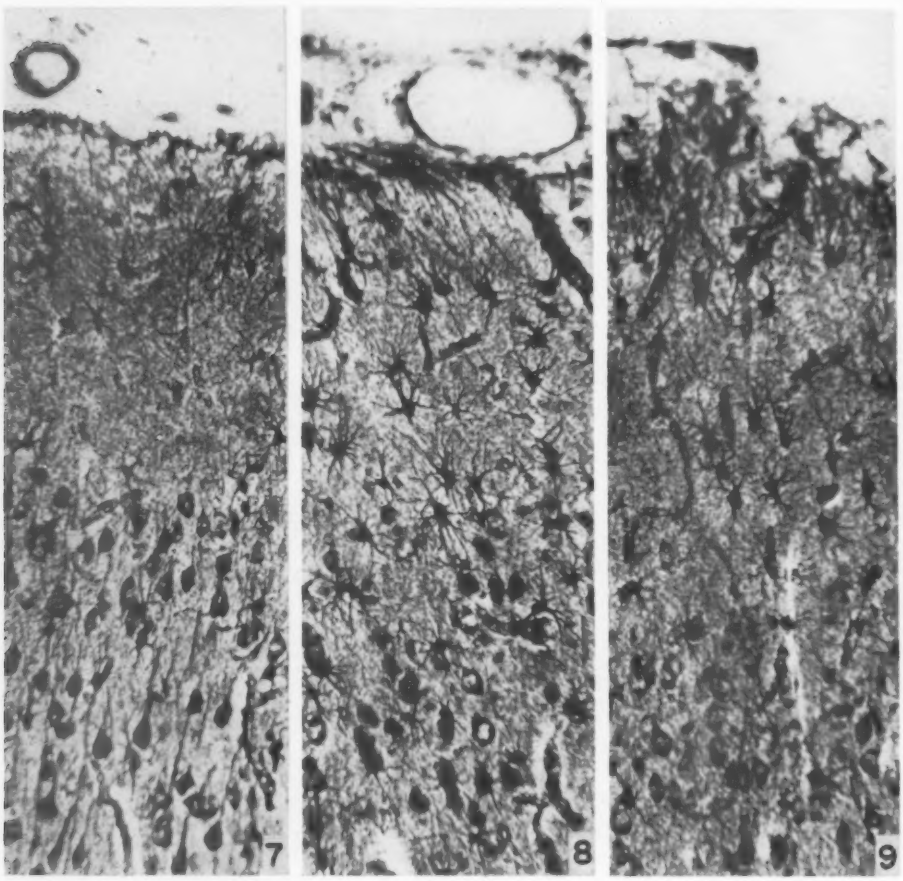


FIG. 7.—Exposure to air for 30 minutes, sacrificed on the seventh day. (Gold chloride 680 x)

FIG. 8.—Exposure to ultraviolet radiation 30 minutes, sacrificed on the seventh day. (Gold chloride 680 x)

FIG. 9.—Exposure to ultraviolet radiation 1 hour, sacrificed on the seventh day. (Gold chloride 680 x)

In none of the exposures to ultraviolet radiation or air were there changes in the oligodendroglia.

In the animals which were exposed to ultraviolet radiation for 30 minutes and sacrificed at the end of 28 days (Fig. 10) there was a marked regression of the changes noted at the end of seven days. In these specimens there was a

slight thickening of the arachnoid but no cells were present in the subarachnoid space. The neurons (Fig. 11) had practically assumed their normal form except for a few shrunken cells still present in the superficial layers of the cortex. There remained a slight patchy decrease in the number of neurons, with occasional neuronaphagia. There was also still noted a slight increase in the astrocytes in the marginal layers.

The control animal which was anesthetized for three hours and not exposed to air or ultraviolet radiation failed to show any microscopic changes.

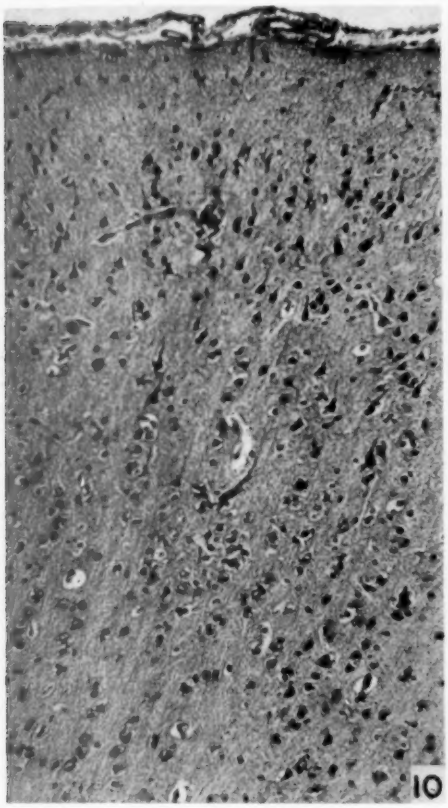


FIG. 10.—Exposure to ultraviolet radiation 30 minutes, sacrificed the twenty-eighth day. (Hematoxin phloxine 125 x)

FIG. 11.—Exposure to ultraviolet radiation 1 hour, sacrificed the twenty-eighth day. (Toluidine blue 660 x)

COMMENT

Prados, Strowger and Feindel[9] reported in detail the reaction of the brain to air exposure. Our control animals verified their findings although the exposure time was shorter. The changes produced by ultraviolet radiation are similar to those which occur with air exposure but they occur much sooner.

It is our opinion that there is no contraindication to the use of ultraviolet radiation in the operating room if the usual neurosurgical technic of pro-

tecting the exposed and uninvolved cortex is followed. The changes which do occur with a 30-minute exposure are regressive and this time interval should be sufficient to inspect the cortex and remove a lesion if the uninvolved cortex is kept covered with moist cottonoid strips. This statement is also borne out by the fact that from a clinical standpoint we have never observed a postoperative reaction which we could attribute to the ultraviolet radiation. From our experiments one must however warn against its use when it is necessary to keep the brain exposed for long periods of time while stimulating the cortex to locate an epileptic focus or in the course of obtaining electroencephalograms from the cortex.

We have not had the opportunity to study its effects upon the human brain except in three cases of topectomies. In these cases the area to be resected on one side was exposed to ultraviolet radiation for 45 minutes immediately before removal. There were no cellular changes noted in these cases. No case had presented itself in which we have felt justified in exposing the cortex and waiting several days before doing the resection.

SUMMARY

The effects of ultraviolet radiation upon the exposed cortex first appear in approximately 30 minutes and become more pronounced as the length of time is increased. These changes consist of a meningeal reaction with thickening of the arachnoid, the appearance of red and white blood cells in the subarachnoid space, a dilatation of blood vessels, an increase in the size of the perivascular and perineuronal spaces, the shrinkage and chromatolysis of the neurons and an increase in the size and number of the astrocytes. These changes were also noted in the brains of the animals which were exposed to air alone but they were not as marked and took a longer exposure time before they appeared. The changes in both instances become regressive if not carried beyond a certain exposure period of approximately 30 minutes.

We feel that no contraindication exists to the use of ultraviolet radiation in the neurosurgical operating room if the uninvolved cortex is protected with the same meticulous care that is mandatory in all modern neurosurgical procedures.

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DISARTICULATION OF AN INNOMINATE BONE
(HEMIPELVECTOMY)
FOR
PRIMARY AND METASTATIC CANCER*†

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INTRODUCTION

The radical resection of an innominate bone, its contiguous soft tissues and the subjacent lower extremity as a means of ablating cancer, has received recently renewed interest.[1, 2, 3, 4, 5, 6]

The decreasing mortality rate attendant upon the performance of this procedure has removed the diffidence which previously has been associated with hemipelvectomy. Moreover, as increasing knowledge is obtained of the natural history of certain forms of cancer and as the more conservative methods of therapy are evaluated, the status of this operation in our present surgical armamentarium can be determined.

Since the first successful resection by Girard in 1895[7] 158 resections have been recorded. The efficacy of any surgical procedure can be determined by evaluating reported mortality and survival rates.

The purpose of this presentation is to record our experience with eight patients who were subjected to radical exarticulation of the lower extremity through the sacroiliac synchondrosis.

Although the period of follow-up is still too short to permit final evaluation, certain lessons could be gleaned by the study, and though the number of cases of this series are few, they constitute, nevertheless, the largest series in the American literature to date.

Definition. Hemipelvectomy (disarticulation of innominate bone) refers to that surgical procedure in which the entire innominate bone, contiguous somatic tissues (buttock), and entire subjacent lower extremity are resected en masse. Because the cancellous nature of the innominate bone favors the wide dissemination of cancer throughout its structure, the entire bone should be

* Submitted for publication, December, 1948.

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removed.[1, 2] Not infrequently it is necessary to resect such other viscera as peritoneum, testicle and spermatic cord structures (Case 7), intra-abdominal viscera,[8] and periaortic lymph nodes (Case 8).

Synonyms. There is little unanimity of terminology regarding this operation. The procedure of radical resection of an innominate bone and lower extremity has been variously described as interiliosacropubic amputation,[9, 16] transiliac amputation,[11] interinnomino-abdominal amputation,[3, 18] intrapelvia-abdominal amputation,[14] interpelvi-abdominal amputation,[13] hindquarter resection,[7] ilio-abdominal amputation,[10] sacroiliac disarticulation, interilioabdominal amputation,[12, 23] and hemipelvectomy.[21, 22] For the purpose of this discussion, the authors prefer the term hemipelvectomy.

Historical. An excellent review of the historical development of the operative procedure from the first attempt by Billroth in 1891 is presented by Gordon-Taylor and Willis.[3] Following Billroth's experience, several unsuccessful resections were attempted, and in 1895 Girard performed the first successful resection.[7] Pringle in 1916 presented his experience with four cases.[13] In 1935 Gordon-Taylor and Willis recorded five instances where transiliac resections were performed,[3] and in 1946 Gordon-Taylor and Patey presented the records of 21 personal cases (the largest series reported) and reviewed the literature to that year.[4] Morton introduced the procedure to America.[5] Sugarbaker and Ackerman (6 cases)[1] and Pack and Ehrlich (6 cases)[2] have presented the most recent experience with this operative procedure.

INDICATIONS

Hemipelvectomy is indicated for those neoplasms which involve the hip joint, pelvic parietes, or soft tissues of the iliac region, and which cannot be surgically extirpated by more conservative methods. The following tabulation classifies the various conditions where this procedure may be indicated.

(1) Primary malignant neoplasms of the innominate bone such as osteogenic sarcoma, and periosteal fibrosarcoma.[2]

(2) Primary malignant neoplasms of the femur which have invaded the hip joint. (Case 6.)

(3) Cancer of the soft somatic tissues of the upper thigh, inguinal region, or buttock, which have invaded the hip joint or extended through the obturator foramen to involve the pelvic parietes.

(4) Metastases to the iliac region which have infiltrated the hip joint, the pelvic parietes, or which, because of local extension, have precluded extirpation of the disease by less radical procedures such as radical groin dissection, and so forth. In this group are included:

(a) Metastases from primary epidermoid carcinomas or sarcomas of the lower extremity. (Case 8.)

(b) Metastases from malignant melanoma which cannot be treated by hip joint disarticulation or radical groin dissection.

(c) Metastases from carcinoma of the penis (Case 2) or rectum in certain selected cases.

(d) Metastases from certain distant primary tumors, as kidney carcinoma (Case 7) or thyroid carcinoma.[5]

In all instances where the resection is performed for the treatment of metastases, the primary neoplasm must be controlled or controllable.

(5) Certain massive benign tumors of the innominate bone, as chondroma,[6] osteochondroma,[14] or of the somatic tissue of pelvic area (neurofibroma)[2] if they cannot be resected adequately by other less radical procedure.

(6) For palliation in certain instances of generalized metastases: melanoma (Case 5), Kaposi's hemorrhagic sarcoma,[2] spindle cell sarcoma[4] where the lesion of the groin produces a bulky infected and painful mass, which cannot be controlled by any other modality.

(7) Certain infections and trauma,[4, 5] which will not be discussed in this presentation.

In this series the resections were performed for synoval sarcoma, fibrosarcoma, periosteal fibrosarcoma, iliac metastases from a primary squamous carcinoma, Ewing tumor, and metastatic hypernephroma. One palliative resection was performed for melanosarcoma.

SURGICAL PROCEDURE

Preoperative preparation. The adequate control of fluid, electrolyte, and colloid balance as for any major surgical procedure and correction of anemia and other metabolic abnormalities are imperative.

The patients are placed on an antibiotic regime (penicillin, 50,000 units every four hours) one week before surgery. Two days before surgery they receive streptomycin (1 Gm. each day) and the day before operation, 6 Gm. of sulfadiazine is administered. The evening before operation a gentle enema is given.

All of the patients were males, hence we have had no experience with vaginal preparation. However, thorough cleaning of the vagina is recommended.[5]

Preoperative debridement, or cautery excision of certain lesions as described by Pack and Ehrlich,[2] in our experience is unnecessary. In bulky fungating tumors a small drape is sutured over the lesion at the time of surgery. An indwelling urethral catheter is inserted before the patient comes to the operating room.

Preoperative preparation of the psyche of all candidates for this operation is rewarded postoperatively by a grateful patient who bravely resigns himself to the deformity. None of our patients regretted their decision to submit to this surgical procedure.

Anesthesia. Endotracheal inhalation anesthesia (nitrous oxide, oxygen, and ether) was used in the earlier cases. Recently a combination of Baird's solution* and nitrous oxide has been found a very satisfactory anesthetic agent. The patient can be moved easily when necessary and this mixture is desirable for the hypotension which not infrequently attends the operation.

* A solution of pentathol and curare containing 25 milligrams of sodium pentathol and 5 units of d-tubocurarine chloride per cubic centimeter.

Technic of Operation. The operative area is prepared with zephiran, the anal opening is closed with sutures, and the scrotum is fastened to the opposite thigh with a few silk sutures.

The patient is placed on the table in a tilted position with his involved side supported on a kidney rest. The involved extremity is slightly flexed at the hip and knee, and is externally rotated and abducted.

Incision. The incision extends from the symphysis pubis, parallel to the inguinal ligament, to a point two centimeters superior to the anterior superior iliac spine. Through this incision the entire anterior dissection is accomplished.

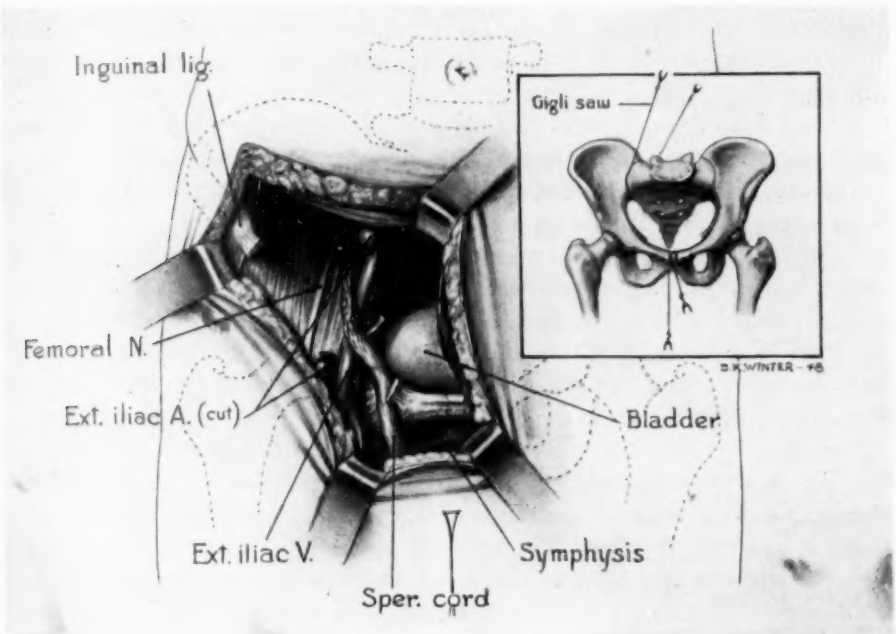


FIG. 1.—*Anterior Dissection.* The incision which extends from the symphysis pubes to 2 cm. superior to the anterior superior spine of the ilium has been deepened. The inguinal ligament severed at its attachments and the external iliac artery ligated and clamped. After retracting the spermatic cord structures and bladder, the external iliac vein will be ligated and divided, the crest of the ilium and sacroiliac synchondrosis skeletonized by dividing the overlying muscles and the innominate bone disarticulated (insert).

The incision is then curved posterior and inferior, over-riding the greater trochanter and extending along the infragluteal fold to join the anterior incision at the symphysis pubes.

This incision extends more superiorly than that usually described[2, 13] and it permits good retraction of the peritoneal contents out of the field of surgery. It affords an excellent exposure for exploratory celiotomy when indicated (Case 3) and permits resection of the periaortic lymph nodes to the level of the renal vessels (Case 8).

Anterior dissection. (Fig. 1) After deepening the anterior incision Pou-

part's ligament is divided and the inferior insertion of the rectus abdominis is severed from the pubic bone. The peritoneum is easily separated from the iliac fossa and the spermatic cord, bladder and rectum are then retracted out of the field and the ureter identified. The external iliac artery and vein are clamped, cut, and doubly ligated.

The practice of postponing ligation of the iliac vein in order to permit the salvage of blood from the lower extremity[2] is not recommended, because the trauma incident to operative manipulation may contribute possibly to intravascular dissemination of the neoplasm, especially in lesions about the vessels. Accordingly, after ligating the external iliac artery just inferior to the bifurcation of the common iliac artery, the involved extremity is raised for a few moments to permit some blood drainage and the external iliac vein is doubly ligated and severed.

The crest of the ilium is skeletonized after severing the iliopsoas muscle high and the bony attachment of the quadratus lumborum muscles. After severance of the iliacus, Gemelli, pyriformis and levator ani muscles, the sacro-iliac synchondrosis is exposed.

The symphysis pubis is now skeletonized and transected with a Gigli saw and the sacro-iliac synchondrosis is next divided by means of a Gigli saw inserted through the sciatic notch.

In certain instances where difficulty may be encountered in inserting the saw through the sciatic notch, this phase of the operation may be postponed until the posterior dissection. After the sacroiliac synchondrosis is skeletonized by severing the posterior musculature, it can be easily transected by means of the Gigli saw passed through the sciatic notch. During our first four procedures a chisel was used to separate the sacroiliac synchondrosis but it was found that a saw is much less traumatic. The actual disarticulation appears to be a critical point of the operation and at this point three patients of the eight suffered marked drops in blood pressure. Accordingly, when the actual disarticulation is to be performed, the anesthetists are instructed to administer whole blood at a brisk rate.

Bleeding from the exposed bone edges is controlled with Gelfoam or bone wax.

Posterior dissection. The patient is turned laterally to the uninvolved side and the posterior phase of the operation is performed. The gluteal muscles, the sacrotuberous, iliolumbar and sacrospinalis ligaments are severed. The gluteal and obturator vessels are identified and ligated. Manipulation of the extremity during the posterior dissection facilitates identification of the various structures. The nerves of the lumbar and sacral plexus are transected when encountered and are not injected. The extremity is now attached only by the sciatic nerve which is severed last.

The skin edges are approximated with number 2 silk sutures, and a drain inserted through a stab wound. A pressure bandage is applied. Split thickness skin grafts may be applied directly if the loss of skin precludes primary closure.

In those instances where there is certainty that the skin of the lower extremity is not diseased, dermatone drums of skin are removed from the resected

specimen and preserved in the ice box. Then if wound breakdown does occur, skin is available for grafting. This method was utilized with success in Case 4.

Postoperative care. After removing the temporary anal suture, a rectal tube is usually inserted for the first two days postoperatively.

Tidal bladder drainage is instituted and continued for about four days.

The patient remains on a full course of antibiotics and Wangensteen drainage via a Levine tube in the stomach is routinely used during the immediate postoperative period.

Frequent and large transfusions may be necessary to combat an anemia which may be quite severe. The anemia results not only from the operative loss of blood but also the removal of a large amount of erythropoietic tissue. The anemia has not persisted longer than two weeks in this series.

Early ambulation is encouraged and the patient instructed how to bear all weight on the one ischial tuberosity.

Postoperative complications. (1) *Genito-urinary and gastro-intestinal.* There have been no complications in the normal activity of urination or defecation. In one patient (Case 4), the posterior wound was drawn taut placing the anus on a bias but this did not produce any discomfort. No bladder or rectal infections developed. Prophylactic use of Wangensteen suction prevented abdominal distention.

Any existing sexual function has not been compromised in any patient in this series. The wife of one patient is now pregnant.

Judin's patient became pregnant and had a normal delivery following the operation.[10]

(2) *Phantom limb.* This objectionable complication was encountered in four patients of this series. Usually the degree of symptoms before surgery dictated the severity of "phantom limb" pain. One patient (Case 5) on whom the operation was performed for palliation suffered so severely from phantom limb pain that any benefit from the operative procedure was negated.

(3) *Herniation.* No hernias have been observed in this series. The peritoneal cavity is well supported by fascia and skin; hence the retention of the gluteus maximus for this purpose or the utilization of other supporting measures is not necessary.[16]

Wound separation and postoperative infection. This has been the most frequent complication encountered in our series, occurring in four of the eight operations. In three cases a rapid healing occurred which appeared complete in ten days after surgery. In three patients (Cases 2, 5, and 7) the complication can be attributable to the fibrosis and compromise of healing ability of tissue resulting from previous irradiation.

In no instance did the wound separation and corresponding local infection produce severe complications and in all instances the infection was satisfactorily controlled and the wound secondarily closed with the aid of skin grafts.

Osteomyelitis. Pack and Ehrlich caution against severing the pubic bone anywhere except through the symphysis because the exposed cancellous bone may be a locus for future infection.[2]

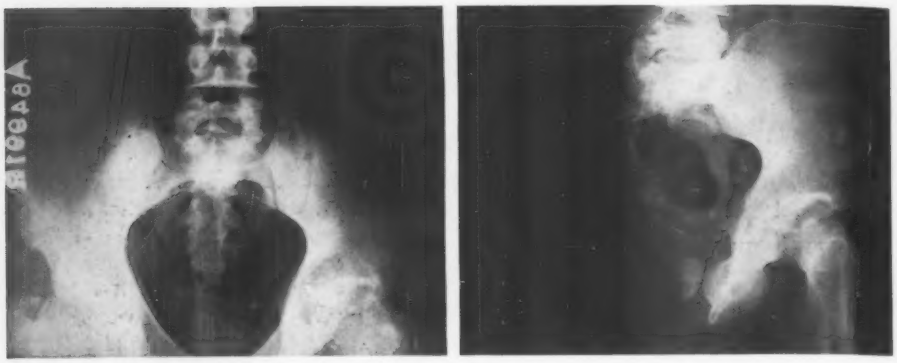


FIG. 2.—*Case 1.* Roentgenogram of pelvis demonstrating osteolytic lesion of right ilium resulting from an Ewing Endothelioma. The photograph on the right is a postoperative roentgenograph demonstrating absence of right innominate bone.

FIG. 3.—Surgical specimen of Case 1. Bulky Ewing Endothelioma arising in the ilium and infiltrating gluteal region.

CASE REPORTS

Case 1.—C. R.—Ewing tumor involving right buttocks and ilium.

The patient is a 26-year-old white male who noted rapid fatigability and vague pains in the right lower extremity of four months duration. There was in addition, swelling of the right buttock of two months duration. The patient had no other symptoms.

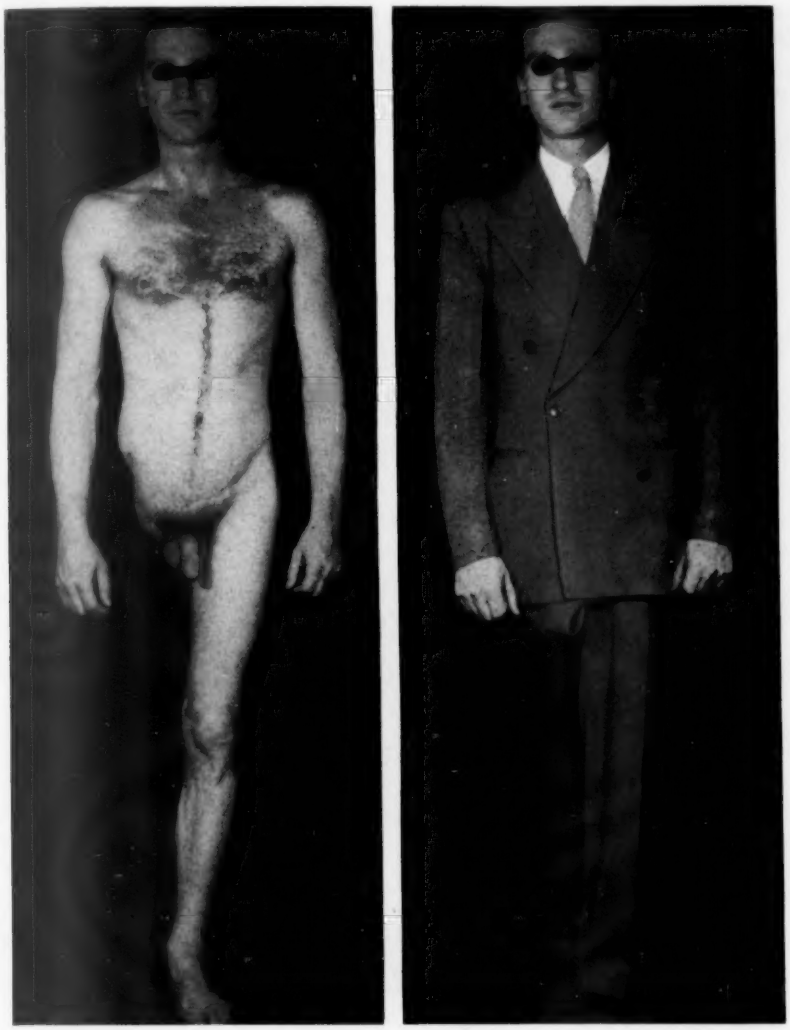


FIG. 4.—Photograph of patient (Case 1) five months following hemipelvectomy.

Physical examination on September 12, 1946, was negative except for a large, diffuse non-tender mass involving most of the right gluteal region and measuring 8 x 12 cms. The overlying skin was distended and of a pinkish hue.

Radiographs revealed invasion of the right ileum extending toward but not involving sacro-iliac synchondrosis (Fig. 2). Roentgenograms of the chest were negative for metastases and all laboratory studies were within normal limits.

A biopsy of the gluteal mass was reported anaplastic sarcoma.

On October 28, 1946, a right hemipelvectomy was performed and the patient made an uneventful postoperative recovery. The resected specimen revealed the entire right posterior region to be replaced by a hemorrhagic, partially necrotic mass with poorly defined borders (Fig. 3). The iliac bone was invaded by tumor.

The patient remained asymptomatic but on July 22, 1947, follow-up roentgenograms of the chest revealed bilateral metastasis. He was given a course of Coley's toxin therapy consisting of 14 daily intravenous injections of the toxin, starting November 8, 1947. The initial dose was 1/100 minum and succeeding doses were gradually increased until a maximum dose of four minums was reached which was repeated four consecutive days. Roentgenograms revealed an increase in the metastatic deposits in the lungs. He remained asymptomatic until April 8, 1948, when he developed a persistent, productive cough, right chest pain, and dyspnea. Thoracentesis yielded 3240 cc. of hemorrhagic fluid.

This patient is living at the present time with bilateral pulmonary metastases. He is relatively asymptomatic but is receiving deep roentgen ray therapy to the pulmonary metastases.

FIG. 5.—*Case 2.* Preoperative appearance one and one-half years after partial amputation of penis for carcinoma and repeated fulgerations and x-ray treatments to metastases in right groin which were deeply infiltrative. Left inguinal nodes also contain metastases.

Comment. An attempt to treat a massive Ewing's tumor by radical surgery succeeded in controlling the primary lesion but pulmonary metastases became clinically manifest nine months after the resection.

The patient is relatively asymptomatic one year and nine months subsequent to operative intervention and one year after the appearance of pulmonary metastases.

Case 2.—J. P. Right hemipelvectomy and radical groin dissection of opposite side for metastases from carcinoma of penis.

The patient, a 54-year-old colored male, was admitted to the hospital in February, 1946, with a diagnosis of carcinoma of penis with right iliac lymph node metastases. He

was treated by a partial amputation of the penis and deep x-ray therapy and fulgeration were administered to the iliac metastases. During the subsequent year and a half, repeated attempts to control the metastases with irradiation and cautery excision were without benefit.

FIG. 6.—*Case 2.* Gross appearance of operative specimen demonstrating infiltrating metastases.

When first observed by the authors on February 24, 1947, the patient presented a large mass involving most of the right groin and measuring 10 cm. in diameter. It was hard and board-like in character. It was intimately bound to the underlying structures,

and presented the appearance of carcinoma and X-radiation reaction. In the center of the board-like area was an ulceration measuring 3 cm. in diameter, consisting of a dirty grey foul granulating surface. (Fig. 5)

In the left inguinal region were many hard freely movable lymph nodes measuring 2 to 4 cm. in diameter.

The patient refused surgery but returned four months later with the right groin severely infected. After a careful preoperative regime, a right hemipelvectomy was performed on July 28, 1947. The patient went into surgical shock during the operation which was combatted by transfusions. His postoperative course was uneventful.

The superficial and deep iliac nodes were found involved by metastases. The neoplasm had extended to the soft tissues of the groin and had extensively infiltrated the contiguous muscles. (Fig. 6). The irradiation fibrosis obscured the planes of clearage.

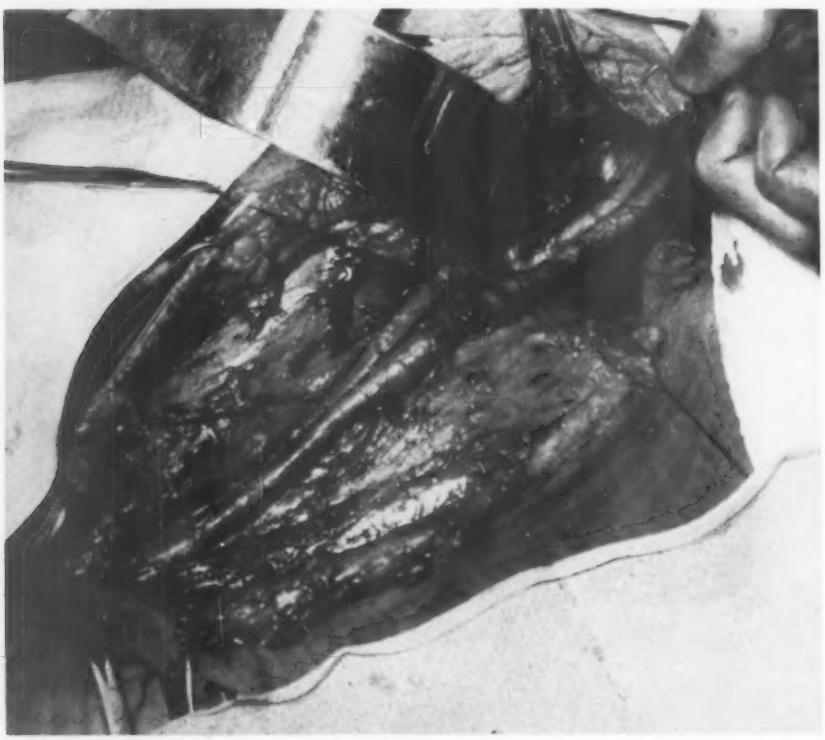


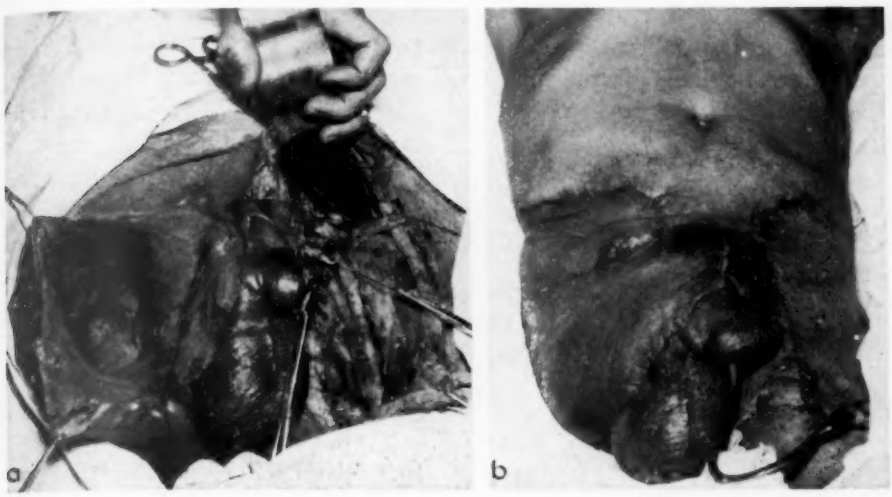
FIG. 7.—*Case 2.* Left radical groin dissection demonstrating iliac and femoral vessels and the inguinal region stripped of lymph node metastases.

Postoperatively he developed a slough of the flaps and wound infection. It was felt that the repeated attempt at cautery excision and the deep irradiation contributed to the slough.

He was given supportive therapy, antibiotics, and moist dressings which controlled the infection.

On August 21, 1947, a left radical groin dissection and closure of the defect resulting from the right hemipelvectomy was performed. Superficial and deep iliac lymph nodes were found infiltrated with cancer. The procedure was tolerated well (Figs. 7 and 8) and the resultant defect in the suprapubic area was closed with a split thickness dermatome graft.

At the present time, this patient is clinically free of tumor.



A B

FIG. 8.—*Case 2.* (A) Left radical groin dissection and opened wound from previous right hemipelvectomy prepared for closure. (B) The closure has been completed.

FIG. 9.—*Case 3.* (A) Operative specimen demonstrating testicle, spermatic cord and portions of peritoneum which were infiltrated by the bulky synovial sarcoma.

Comment. This represents a case of squamous carcinoma of the penis treated primarily by partial amputation of penis. Two years later a right hemipelvectomy and left radical groin dissection were performed for persistent tumor. Bilateral groin metastases have remained controlled for one year. Previous attempts to treat the groin metastases with irradiation and local excision were without effect.

FIG. 10.—*Case 3.* (B) Postoperative photograph demonstrating the high incision necessary to resect involved peritoneum. Slight separation of wound edges occurred.

Case 3.—P. A. W. Synovial sarcoma of right upper thigh.

This patient was a 36-year-old white male who first noted a walnut sized mass in the right upper thigh in 1945. It remained quiescent for one year and on November 7, 1946, a local excision was performed elsewhere, followed by postoperative irradiation. The factors of irradiation are not known. An ulcerated area of the upper thigh persisted and an inguinal mass subsequently developed.

The patient was admitted to Veterans Administration Hospital, Hines, Illinois, March 24, 1947, at which time he presented an ulceration 2 cm. in diameter, 6 cm. inferior to Poupart's ligament. A subcutaneous mass was present in the subinguinal area. Numerous enlarged superficial inguinal lymph nodes were palpable. The tumor extended above Poupart's ligament for an indeterminate distance. A biopsy was interpreted as synovial sarcoma. All laboratory findings were normal and a chest roentgenogram negative for metastases.

Operation. A hemipelvectomy was performed on April 23, 1947. It was noted that cancer had grossly invaded all deep iliac lymph nodes and infiltrated into the peritoneum. Large masses of friable intra-abdominal tumor tissue were resected including the peritoneum; part of prostate, spermatic cord structure, and testicle. (Fig. 9.)

The patient tolerated the operative procedure well and his immediate postoperative course was uneventful except for slight necrosis of the posterior skin flap (Fig. 10). Two weeks postoperatively he developed evidence of intraabdominal cancer and succumbed July 3, 1947, due to generalized visceral metastases.

Comment. A malignant synovial sarcoma of the thigh had produced diffuse generalized visceral metastases from which the patient succumbed two months following hemipelvectomy.

Case 4.—T. G. Fibrosarcoma left iliac region unsuccessfully treated by irradiation. This 51-year-old white male dated the onset of his symptoms from March, 1946, when he noted a vague aching in upper left thigh region. Two months later he noted a

FIG. 11.—*Case 4.* Photograph demonstrating increased circumference and ulceration of left thigh due to diffuse fibrosarcoma which infiltrated to the hip joint. Previous irradiation therapy had been administered.

gradual increase in the circumference of the thigh. There was no weight loss. Biopsy of the left thigh established the diagnosis of fibrosarcoma. The patient was given thirty deep x-ray treatments elsewhere during August and September, 1946, with mild relief. (The irradiation factors could not be obtained.)

On admission to the hospital February 1, 1947, the patient was well nourished but there was a diffuse, firm enlargement of the upper left thigh. The skin over this area was pigmented. There was a shallow ulceration 2 cm. in diameter with sloping margins and a dirty grey base on the anterior aspect of the pigmented area (Fig. 11). All laboratory data was negative and chest x-rays revealed no evidence of pulmonary pathology.

On February 17, 1947, a left hemipelvectomy was performed and a large tumor mass

involving the musculature of the upper thigh, extending inside the retroperitoneal area and intimately adherent to the external iliac vessels.

The patient tolerated the procedure well but developed postoperative separation of the wound edges necessitating skin grafting.

On May 15, 1947 (three months postoperatively) the patient developed cough and chest pain. Pulmonary metastases were demonstrated by roentgenographic studies. Palliative irradiation was without effect and the patient succumbed July 10, 1947. Autopsy revealed massive hemorrhagic pulmonary metastases involving approximately two-thirds of the pulmonary parenchyma. No signs of any other cancer were observed.

Comment. A fibrosarcoma of left thigh was treated by irradiation without effect. Six months after irradiation therapy a hemipelvectomy extirpated the local disease but the patient succumbed five months postoperatively due to pulmonary metastases. It is of interest to conjecture what the preoperative delay may have contributed to the final outcome.

Case 5.—J. D. Palliative resection for diffuse melanosarcoma.

The patient is a 28-year-old white male. He had a small brown mole measuring ½ cm. in diameter on the anterior lower right leg locally excised in October, 1945. The excision was incidental to reconstructive surgery which was performed in Luzon subsequent to gunshot wounds to the right leg.

One year later a mass developed in the right inguinal region which had gradually increased in size. The inguinal mass was excised and the diagnosis of "cancer" made. Five x-ray treatments were given but the factors of irradiation are not known. However, the mass in the inguinal region grew rapidly in size and the patient developed numerous painless subcutaneous nodules varying from 1 to 3 cm. in diameter.

On admission, June 12, 1946, the patient presented a large irregular tender, hard, and fixed mass in the right inguinal region. It was firmly attached to all surrounding structures and the overlying skin was telangiectatic, erythematous and shiny. The area was exquisitely tender. The patient also presented numerous subcutaneous nodules. He was emaciated and in extreme pain. The following palliative procedures were attempted: (1) Vigorous estrogenic therapy, (2) a course of methyl-bis (nitrogen mustard) therapy and (3) local deep x-ray therapy. The severe pain in the groin, radiating down the leg, persisted.

Accordingly, on July 30, 1947, a palliative right hemipelvectomy was performed and the patient made an uneventful postoperative recovery. However, the symptoms due to the "phantom limb" vitiated any benefit from operative procedure. The patient succumbed from generalized melanosarcomatoses on September 28, 1947.

Comment. A palliative procedure was performed and a foul smelling, ulcerated infected tumor was removed which had caused the patient severe pain that did not respond to medical management.

The ensuing phantom limb negated most of the benefits expected from the resection.

Case 6.—E. C. R. Periosteal fibrosarcoma of right femur.

This 26-year-old white male was perfectly well until May, 1946. While in China with the Marines, he noted pain in the right hip and immediately consulted his surgeon. Two weeks later the pain which had previously been localized to the hip began to radiate down the leg to the knee, causing limited motion of the right knee and hip. In January, 1947, x-rays were taken and diffuse osteoporotic lesion was diagnosed "septic arthritis." The hip and knee were then placed into a cast. In February, 1947, the patient complained of severe pain in the chest, and fever. He was hospitalized for two months and treated

with penicillin and was said to have had pleurisy. At that time he lost 20 pounds of weight in two months. In April, 1947, because of the persistence of difficulty with his hip joint and leg he was placed in a body brace. In May, 1947, x-rays were taken and the osteolytic lesion of his hip was said to have extended and the patient was placed in a plaster spica. In July, 1947, repeated x-rays were taken which showed osteolysis of the right hip. An aspiration biopsy was taken on July 15, 1947, and an immediate pathological report was obtained of sarcoma, either a fibrosarcoma or a synovial sarcoma. X-rays of the right hip revealed a marked osteolytic lesion involving the head and neck of the femur (Fig. 12).

FIG. 12.—*Case 6.* Roentgenograph demonstrating infiltration of fibrosarcoma into hip joint and femur.

Physical examination revealed a large mass in the right inguinal region. The overlying skin was neither adherent nor invaded. The mass extended to involve most of the hip joint, extending to Poupart's ligament and to the anterior surface of the right upper thigh. Along the margin of the mass a small freely movable lymph node was palpated.

A hemipelvectomy was performed on July 21, 1947. The resected specimen presented a large circumscribed mass which was greyish in color and involved most of the retroperitoneal space, invading the anterior musculature of the thigh. (Fig. 12). The tumor mass infiltrated the neck and head of the femur and involved the acetabulum. The patient withstood the procedure well and remained asymptomatic except for pain of unknown etiology in the left hip until September 18, 1947, when he developed an acute hepatitis from which he recovered.

In January, 1948, the patient developed chest pain, a dry unproductive cough and dyspnea. A roentgenogram of the chest revealed a massive left pleural effusion and

multiple metastases to the right lung. He was given a course of Caley's toxin with little relief. Repeated thoracentesis yielded large quantities of serosanguineous fluid.

The patient succumbed April 9, 1948, and autopsy revealed massive pulmonary metastases. No evidence of local recurrence was observed.

Comment. Disarticulation through the sacro-iliac synchondrosis was necessary to remove this neoplasm which had invaded the hip joint. Although the neoplasm was surgically resectable, death occurred 8 months postoperatively

FIG. 13.—*Case 6.* Operative specimen showing bulky fibrosarcoma which had invaded hip joint.

due to extensive pulmonary metastases. It is lamentable that one year elapsed from the onset of symptoms until the patient received definitive treatment.

Case 7.—B. L. M. Metastatic hypernephroma.

The patient was a 48-year-old white male who first noted pain in the region of the left hip on weight bearing, in November, 1946. He was treated with various non-specific remedies until June 7, 1947, when roentgenographs revealed a destructive process of the left ilium. A biopsy specimen was interpreted as sarcoma; either reticulum cell sarcoma

FIG. 15.—*Case 7.* Photograph of innominate bone which has been detached from the remainder of the surgical specimen demonstrating the osteolytic metastatic hypernephroma.

FIG. 14.—*Case 7.* Roentgenogram of pelvis demonstrating osteolytic character of a metastatic hypernephroma.

or angiosarcoma. The patient was given a course of deep x-ray therapy from July 10, 1947, to August 14, 1947, for a total dose of 3,000 roentgens to the left ilium posterior and 3,000 roentgens to left lateral ilium with the following factors: 250 KV, 2 mm. copper filtration, 80 cm. target skin distance, estimated tumor dose 3675 roentgens, with slight regression in the size of the mass.

On October 1, 1947, a left hemipelvectomy, which included a portion of the sacrum, was performed. The resected specimen demonstrated a large mass of hemorrhagic neoplastic tissue measuring 8 x 7 centimeters and destroying the ilium (Fig. 15). Microscopic sections from the surgical specimen revealed the neoplasm to represent a metastases from a primary kidney carcinoma.

The patient has made an uneventful postoperative recovery with the exception of a painful sinus which was debrided and healed completely. At present the patient reveals no evidence of disease. Complete genito-urinary studies, including peri-renal air insufflation are normal.

Comment. Radical surgery was performed on this patient because of the mistaken impression that the neoplasm of the ilium was primary in bone. Careful study by several pathologists revealed the neoplasm to be a metastases from a primary renal cancer. The patient is well one year postoperatively. It is planned to explore the kidneys.

This case resembles Sugarbaker's and Ackerman's case number 3.[1]

Case 8.—Squamous carcinoma of left lower leg, developing on a burn scar and producing fixed superficial and deep inguinal metastases.

The patient was a 24-year-old white male who suffered gasoline burns of lower left leg, right thigh and left lower arm in 1936. The wounds required two years to heal and he remained well from 1938 to 1947, at which time the scar of the left lower leg ulcerated and the ulcerated defect continued to enlarge.

He was hospitalized elsewhere for 142 days receiving local treatment, attempts at plastic repair and a simple excision of lymph nodes in the left inguinal region.

On admission to University Hospitals, University of Minnesota, on August 8, 1948, he presented a large fungating tumor mass measuring 23 x 12 x 1 cm. and extending from the left popliteal space inferiorly to involve most of the left lower leg. The surface was granular with heaped up edges. Biopsies from various areas were reported squamous carcinoma.

In the left inguinal region were numerous firm fixed masses which measured 3 to 4 cm. in diameter. They had coalesced to produce a large irregular mass. There was a recent surgical scar over this inguinal mass.

The patient presented, in addition, old burn scars involving the right lower extremity and right upper extremity which were well healed. An inferior venacavogram outlined the inferior vena cava and there was no evidence of extrinsic or intrinsic pressure.

On August 20, 1948, the deep iliac region was explored through an incision which extended from the parallel to the inguinal ligament to a point about 3 cm. superior to the anterior superior spine.

The deep iliac nodes were noted to be infiltrated with cancer and adherent to contiguous structures. Accordingly, a sacroiliac disarticulation was performed in conjunction with Dr. Arnold Kremen. A dissection of the periaortic nodes on the involved side to the level of the renal pedicle preceded the hemipelvectomy.

The patient withstood the procedure well and his postoperative course was uneventful.

The pathologic specimen revealed the deep iliac region involved with a large mass of necrotic tumor tissue which completely surrounded the femoral artery and vein and infiltrated the walls of the vessels. The periaortic nodes did not reveal evidence of cancer and there were no popliteal lymph nodes involved by the neoplastic process.

Comment. A hemipelvectomy was necessary for this squamous carcinoma of the lower leg which developed on an old burn scar and produced superficial and deep iliac metastases which had infiltrated to the soft structures of the pelvis and invaded the walls of the external iliac artery and vein.

DISCUSSION

Operative Mortality. There has been a steady and progressive decline in the operative mortality for hemipelvectomy. In 1909 the mortality rate when performed for cancer was 67 per cent[13] and Pringle in 1916 remarked on the achievement in decreasing the mortality rate to 56.6 per cent in the intervening years.[13] In 1935 the operative mortality of all cases performed to that date was 60 per cent.[3]

In the subsequent ten years, 80 additional cases were collected and the reported mortality rate of that series was 18 per cent.[4]

Recent reports by Morton, 4 cases[5]; Pack and Ehrlich, 7 cases[2]; and this series, 8 cases without an operative death suggests that the technic of conducting the patient safely through a hemipelvectomy has been achieved. Adequate pre-and postoperative care and special emphasis on supportative therapy (transfusion) during the operation, are the major factors contributing to the precipitous drop in the operative mortality rate.

There is nothing to suggest that the patients of the three series cited above were better operative risks than in previously reported series; in fact, two patients were critically ill from widely disseminated cancer and the operative intervention performed for palliation.[2]

PROGNOSIS

In this series the end results are not good. Four patients have succumbed. In one patient where the operation was performed for palliation, the patient succumbed two months postoperatively of diffuse melansarcomatoses.

One patient, who had intraperitoneal invasion of a synovial sarcoma at the time of surgery, expired two months postoperatively with generalized visceral metastases (Case 3).

Two additional patients succumbed five months and eight months postoperatively due to diffuse pulmonary metastases resulting from a spindle cell fibrosarcoma and synovial sarcoma respectively (Cases 4 and 6).

A fifth patient has bilateral pulmonary metastases 24 months subsequent to surgery (Case 1) and the remaining three patients are apparently free of disease two, 12, and 15 months respectively after surgery (Cases 2, 7 and 8).

In none of the patients that expired were local recurrences observed as observed by postmortem examination.

Further review of this series reveals that in all seven cases where the operation was performed for curative purposes, there was a delay varying from seven to 19 months from the onset of symptoms. The average delay of the group was 10.4 months (Table I). Moreover, the delay in certain instances was attributable to the medical profession. In two instances (Cases 6 and 7), a proper diagnosis was not established and no definitive therapy instituted for

prolonged periods. In three instances, adequate therapy was delayed while conservative surgical measures or irradiation therapy were attempted by other physicians (Table I).

It is probable that the delay in addition to the trauma of ineffective therapy contributed significantly to the undesirable results in four patients of this series.

It is difficult to adjudicate the true accomplishment of exarticulation of the pelvis from published reports because of the inadequacy of the data. Pack and Ehrlich state that one-third of the patients who submitted to the operation

TABLE I.— *Résumé of 8 Patients on whom Hemipelvectomy was Performed— Author's Series.*

Patient	Age	Pathologic Diagnosis	Previous Treatment	Delay Before Operation	Duration From Operation Until Metastases Occurred	Remarks
(1) C.R.	26	Ewing's tumor of right gluteal region; and right ilium	None	7 months	9 months	Alive 24 months after operation. Bilateral pulmonary metastases present
(2) J.P.	54	Squamous carcinoma of penis with bilateral groin metastases	(1) Partial amputation of penis. (2) Deep x-ray and cautery excision right inguinal metastases	1 year, 5 mo.	0	Patient well 15 months after right hemipelvectomy and left radical groin dissection
(3) P.A.W.	36	Synovial sarcoma anterior inguinal region	Local excision and deep x-ray.	8 months	2 weeks	Died 2 months after surgery. Duffuse visceral metastases
(4) T.G.	54	Fibrosarcoma anterior inguinal region	Deep x-ray	10 months	3 months	Died 5 months following surgery. Pulmonary metastases
(5) J.R.D.	28	Melanosarcoma generalized	None	Palliative procedure in patient with generalized melanosarcoma		Died 2 months postoperatively. No palliation
(6) E.C.R.	26	Periosteal fibrosarcoma anterior inguinal region	Prolonged symptomatic treatment	12 months	5 months	Succumbed 8 months after surgery from extensive pulmonary metastases
(7) B.L.M.	48	Metastases from kidney carcinoma to left innominate bone	Symptomatic and deep x-ray therapy	7 months		Patient well 12 months after surgery
(8) A.B.	24	Squamous carcinoma of leg with inguinal metastases	Local excision of inguinal metastases	12 months		Patient well 14 months after surgery

because of malignant disease were reported clinically cured, but state further that the follow-up in most instances was most inadequate.[2]

A perusal of the literature reveals nine instances of five-year survivals with the following histologic diagnoses[4]:

Chondrosarcoma	3 patients
Chondroma	1 patient
Osteoclastoma	1 patient
Osteogenic Sarcoma Ilium	1 patient

Extraperiosteal Sarcoma	1 patient
Spindle Cell Sarcoma	1 patient
Epidermoid Carcinoma	1 patient[15]

It is suggested that the low survival rate of reported cases may be the result of the following factors:

1. The previous high operative mortality rate.

2. Certain neoplasms known to be radioresistant (spindle cell sarcoma, synovial sarcoma) received irradiation as the method choice instead of surgical intervention. When hemipelvectomy was instituted finally, there had been a prolonged delay.

3. Conservative surgical procedures were attempted frequently before resorting to radical resection. The less radical procedures were utilized first because (a) they were being appraised, (b) the surgical inexperience of the physician precluded his performing a major procedure, (c) the humane attempt of trying to spare the patient the mutilation resulting from hemipelvectomy and (d) the erroneous policy of trying a more conservative method first to see what it may accomplish before resorting to the radical curative procedure. One may be more conservative in the long run frequently by being radical at the outset.

4. Attempts to retain partial function have led certain surgeons to spare tissue which should have been resected. Sugarbaker and Ackerman[1] stress this feature and have collected from the literature eight patients who developed stump recurrences. They point out that in four cases the innominate bone was incompletely severed and in one instance the gluteus maximus was preserved.

PROGNOSIS AND HISTOLOGIC TYPE

1. Bulky benign lesions such as chondromas, osteochrondromas, neurofibromas, offer the best prognosis.[1, 6]

2. Malignant neoplasms, of low grade malignancy of bone (Chondrosarsoma)[5, 17] or well differentiated malignant neoplasms of soft tissue (myxolysosarcoma periosteal fibrosarcoma, extra-osseous osteogenic sarcoma) should offer a good prognosis.[4]

3. Osteogenic sarcoma of the innominate bone or extension from the femur into the hip bone do not offer a very good prognosis.[23] Cures, however, have been reported.[4]

4. Primary epidermoid carcinoma arising from the skin of the groin and infiltrating deeply[15] or metastases from carcinoma which infiltrate inguinal tissues (Case 2) may offer a good prognosis in certain instances.

5. Sarcoma of soft tissue, especially fibro sarcoma, rhabdomyosarcoma and synovial sarcoma are the histological types for which hemipelvectomy has been performed most frequently and which has produced poor end results. (3 cases of this series) Of 25 cases labelled sarcoma observed in the literature there is only one recorded instance of a five-year survival rate.[4, 14, 18, 21] These figures should not deter one, however, from the performance of radical surgery where it is the only method that may completely extirpate the disease.

6. Hemipelvectomies have been performed for Ewing sarcoma and multiple myeloma, but no cures have resulted.[18, 19]

SUMMARY

In 1916 J. Hogarth Pringle, an English surgeon who pioneered and developed exarticulation of the innominate bone, stated: "There has scarcely been a single operation of any magnitude that has not in the early stages of the development been looked at askance, and the inter-pelvi-abdominal amputation must always remain one of the severest in surgery. But, if the real nature of these cases can be recognized at an early stage and the operation can be carried through before the patients have commenced to run down in consequence of the disease, the mortality following will, I believe, be so far diminished that justification of the operation will in the future be generally admitted."

Pringle's prophecy has been accomplished and inter-pelvi-abdominal amputation is today a safe procedure. Emphasis must be placed on utilizing this procedure with dispatch where indicated.

CONCLUSIONS

1. Disarticulation of an innominate bone and its subjacent extremity have been performed 158 times (exclusive of this report) since the first successful resection 52 years ago.

2. The operative mortality has declined steadily from 67 per cent in 1909 to 56.6 per cent in 1916 to 18 per cent in 1945. In two recent series, Pack and Ehrlich (7 cases) and this report (8 cases), no operative deaths occurred. Careful pre- and postoperative care and adequate transfusions during the operation have contributed significantly toward reducing the hazards of hemipelvectomy.

3. Eight cases where hemipelvectomies were performed to ablate cancer are presented. The preoperative preparation, surgical technic, postoperative complications and their prevention are discussed.

4. The end results of disarticulation of the innominate bone for cancer are not good. Nine instances of five-year survivals are observed in the literature (the follow-ups of many reported cases are not presented frequently).

Of the eight cases reported in the series, one was performed for palliation (melanosarcoma)—one patient succumbed two months postoperatively (synovial sarcoma) from visceral metastases—two patients succumbed from pulmonary metastases (one with fibrosarcoma in five months; and one periosteal fibrosarcoma in eight months)—one patient with Ewing's tumor has pulmonary metastases 24 months following surgery and three patients are apparently free of disease.

Note: Since the manuscript was prepared for publication three additional hemipelvectomies have been performed.

Case 1 is a 35-year-old white male for whom a mid-thigh amputation was performed for a fibrosarcoma about the left knee joint. Because of radiological evidence of sarcoma about the hip joint, a hemipelvectomy was performed and the patient is well and apparently free of disease one year postoperatively.

Case 2 is a 32-year-old white male for whom a hindquarter amputation was performed for a chondrosarcoma involving the head of the left femur and producing a bulky gluteal mass. Symptoms had been present for one and one-half years. The patient is

well six months postoperatively except for a low grade osteomyelitis of the opposite pubic bone.

Case 3 is a 38-year-old white female who weighed 203 pounds. She had pain of the left thigh of two and one-half years duration, and a fracture one year before admission. A massive neoplasm involving the proximal femur, left hip joint, and medial aspect of the thigh necessitated a hemipelvectomy. The histological diagnosis was chondrosarcoma, with invasion of the femoral vein and erosion of femur. Her obesity precluded good wound healing and a period of about two months were required before the patient walked. She is well and apparently free of disease two years after surgical intervention.

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TALC GRANULOMA — A SURVEY OF ITS INCIDENCE AND SIGNIFICANCE*†

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IN THE 14 YEARS since Antopol first described the entity known as talc granuloma, numerous clinical and experimental studies have been reported in the literature. However, there has been an inertia on the part of the medical profession to accept the challenge of the danger of the use of talc. In spite of what has been written practically all hospitals, save those where the problem has been made a special study, are still using talcum powder as a dusting powder for their surgical rubber equipment.

It was not until we had a death at our hospital from intestinal obstruction and fecal fistula directly attributable to talc (reported by Dr. A. J. Swingle[18]), that we became fully aware of the seriousness of the practice of using talcum powder in the operating room. This case instigated our consideration of the statistical incidence of talc granuloma as a postoperative complication. Although a review of the literature revealed many cases resembling those we subsequently found, there was no instance in which a comprehensive survey was made of the incidence of the disease in routine surgical material in a given hospital, to correlate this with total operative procedures performed. With this question in mind we reviewed the consecutive surgical pathologic material submitted to the laboratory over the past 16 months. Not only were we interested in the incidence of occurrence, but also if possible to correlate the presence of talc granuloma with actual morbidity.

HISTORY

It is not the purpose here to completely review the literature on this subject. This has previously been thoroughly done by Seelig *et al.*,[17] and others subsequent to Antopol's first paper in 1933. Knowledge of the effect of talc in tissues has been gradually developed. Erb[3] in 1935 reported six cases of dusting powder granuloma. However, he did not report lesions produced by talc crystals, his cases being due to lycopodium spores. Owen[13] in 1936 reported one case of talc granuloma which caused intestinal obstruction two years following appendectomy. In 1940 German[5] reported a case of lupoid-sarcoid reaction induced by a foreign body (silica) and in 1943 this same author[6]

* Submitted for publication, November, 1948.

† This paper represents part of a thesis submitted by Doctor Ross to the Faculty of the Graduate School of Marquette University in partial fulfillment of the requirements for the degree of M.S. in Surgery.

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presented a series of 50 talc granulomata, 40 of which were intra-abdominal and were found in patients undergoing abdominal surgery for at least the second time. He further found that if serial sections are routinely taken through the omentum of patients previously operated upon, granulomata will almost always be found. In many of his cases the talc was merely an incidental finding and not necessarily the cause of any complaint. Ramsey and Douglass,[14] McCormick and Ramsey,[11] Byron and Welch,[2] and Ramsey[15] all have reported additional cases, and the injury now has been described in various parts of the body, including intra-peritoneal, intra-thoracic and in skin lesions, scar nodules and tumor masses; in vaginal, rectal, brain, spinal, kidney, breast, ovary, testes, penile and parts and in healing surgical wounds, *et cetera,* Lichtman *et al.*[9, 10] found granulomatous lesions in malfunctioning intestinal stomata, and demonstrated experimentally the importance of talc as the causative factor in the production of fistulas. Swingle[18] has reported a case of a patient from this hospital who had a laparotomy for removal of an abdominal tumor and then had 14 subsequent laparotomies and finally expired from intestinal obstruction and fecal fistula caused as a direct result of talc.

PATHOLOGY AND PATHOGENESIS

Talc powder is a hydrous magnesium silicate and contains 82.7 per cent talc, 8.7 per cent calcium carbonate, 7.6 per cent magnesium carbonate, and 1 per cent moisture.[7] Miller *et al.*[12] in 1934 found that quartz, which is 99 plus per cent silica, when introduced into the peritoneum produced nodules that progressively increased in size. This was apparently due to chemical irritation supplied by the solution of silicate in the tissue. Particles below 10 microns in size are particularly harmful to tissues. Talc produces a pseudo-tuberculous, non-caseating, granulomatous type of lesion which previously has been described in pathologic specimens merely as chronic granuloma or chronic foreign body reactions. Lichtman *et al.*[9] point out that "material bleached out of the talc crystals is not the same as the parent substance as the degree of hydration of this derivative substance determines its toxicity." The talc crystals are not inert particles. They immobilize the phagocytes without destroying them, and therefore are not carried into the lymph stream. Usually a circumscribed granuloma is produced at the original site of contamination. Microscopically it is a fibrous granuloma with foreign body giant cell reaction. Under polarized light the smallest talc particles can be seen to be frequently engulfed by large histiocytes, whereas around the larger particles there are typical multinucleated foreign body giant cells.

The role of talc in the actual production of adhesions is a point over which there is marked difference of opinion. From their experimental work, Lichtman *et al.*[9, 10] concluded that simple inoculation of talc with little infection and trauma produced nodules rather than dense fibrosis. This point is interesting inasmuch as German[5] states that talc alone does not cause adhesions; that trauma is necessary to produce fibrin and the talc is incorporated in the adhesions and plays a secondary role. Owen[13] also found that talc injected intraperitoneally in rabbits produced a granulomatous lesion but no adhesions. On the

other hand Lee and Lehman[8] state that when dry talcum powder is dusted over the serosal surfaces without trauma, massive dense uncountable adhesions are produced. It is further interesting to note that as far back as 1934, Bethune[1] described a technic for the deliberate production of pleural adhesions as a preliminary to lobectomy by the use of pleural poudrage with talc. In retrospect it is odd that surgeons using talc therapeutically to produce adhesions did not realize that they were also powdering their gloves with the same substance for operations in which adhesions were not desirable.

Apparently there is extreme variability in the individual reaction to talc. This is seen clinically inasmuch as some wounds with talc fail to heal, or break down within a few weeks following initial healing. In other cases, a period of years may elapse between inoculation with talc and the production of symptoms. The longest time interval between talc contamination and treatment in any of our cases was nine years. Others have reported granulomata developing in scars as long as 36 years after inoculation with talc (Lichtman[9, 10]).

The presence of a talc granuloma does not necessarily presuppose a previous surgical procedure. Cases of dacrocystitis caused by talc have been reported in personnel working in surgical supply rooms where dust counts are extremely high. In one of German's cases[5] the causative agent (silica) was introduced into the tissues when the patient suffered a scalp wound while mountain climbing. Furthermore, granulomatous lesions of the rectum and vagina also may occur after the prolonged use of suppositories coated with talc.

Our own cases, however, all occurred following previous surgery, either at this hospital or elsewhere. The talc crystals may have been deposited into the wound by particles settling from the air—especially inasmuch as we do not have a separate room in which the doctors may "gown and glove"—this being done in the operating room proper. In most cases obviously the source of talc is from the surgeon's glove, both from the outside of the glove as well as following perforation. In a study by Weed and Groves[19] it was observed that in a series of 4,589 operative procedures there was a perforation of one or more gloves in 74.4 per cent of the operations and that 22.6 per cent of the gloves that were used were perforated. Also, the talc may be introduced into the wound on cotton packs and sponges as well as on rubber drains. At this hospital rubber drains were formerly liberally powdered with talc for autoclaving and it is believed that this procedure is carried out in most hospitals throughout the country. Swingle[18] states that regardless of how thoroughly the drains are washed, subsequent examination under the polarizing microscope still reveals birefringent crystals clinging to the rubber.

ANALYSIS OF MATERIAL

Talc crystals were identified by examination under a polarizing microscope. They are seen to be doubly refractile, varying in size up to 10 microns, and of irregular configuration. A positive statement cannot always be made whether or not a given granulomatous lesion is due to talc alone. Although talc can be found in many specimens, it may be merely contributory or incidental and

not necessarily the primary etiologic factor in the production of the granuloma. It was considered significant only when it produced tissue reaction characterized by phagocytosis of the talc crystals by histiocytes and giant cells and by the presence of fibrosis and tubercle formation. Other double refracting substances which must be distinguished from talc include hair, lint, suture material, cholesterol crystals, vegetable fibers, cotton fibers, *et cetera.*

With the above mentioned criteria in mind, a general review was made of 1,912 consecutive surgical specimens submitted to the pathologic laboratory. A total of 33 specimens containing talc granuloma was found. Eight of these were in recurrent pilonidal sinuses, there having been 21 recurrent pilonidal sinuses in the entire series. The remaining 25 specimens (from 21 patients) had been previously identified as nonspecific inflammatory granulomas.

CLASSIFICATION OF CASES

Talc granuloma was found in 33 specimens obtained from 29 patients (Table I). A breakdown of these cases is as follows:

I. Chronic Granulomas as Draining Sinuses: Chest Cases—9.

a. Seven of the granulomas were from five patients with pulmonary tuberculosis, the lesions being a draining sinus tract or chronic granulomatous lesion at the site of a thoracoplasty or a thoracotomy wound, and in one case at the site of a phreniclasia wound. In none of these sections could tuberculosis be found.

b. There were two non-tuberculous chest cases:

(1) One case was a wound granuloma and sinus tract following thoracotomy for empyema from a ruptured amebic abscess of the liver. Four revisions of the wound were required before healing finally occurred.

(2) One case developed a broncho-pleural fistula following a thoracotomy for post pneumonic empyema.

II. Chronic Draining Sinuses and/or Fistulae: Non-Chest Cases—9.

a. Four draining sinuses of the lumbar region all found in second or later operations following an initial operation for (1) shell fragment wound, (2) nephrectomy for tuberculous kidney, (3) lumbar sympathectomy, (4) osteomyelitis of the sacrum.

b. Two fecal fistulae following appendectomy for perforated gangrenous appendices: One of these healed on excision of the sinus tract and repair of the bowel, and the other fistula persisted for four months until the patient died.

c. One pararectal sinus, operated upon five times—(three times at this hospital) before healing finally occurred.

d. One rectal fistula which had been draining since initial surgery two years previously. This patient had pulmonary tuberculosis but no tuberculosis of the rectal lesion was demonstrated on the microscopic section.

e. One case of intestinal obstruction and fecal fistula which caused death of the patient and was directly attributable to talc.[18]

III. Inflammatory Masses:—3.

a. A tumor of the jaw which had progressively enlarged since the patient received initial treatment for gunshot wound of the mandible five years previously.

b. A tumor mass of the right spermatic cord which had developed following herniorrhaphy three months previously. (Hematoma was also a factor.)

c. Talc granuloma superimposed on an angioma which had been partially removed at the initial operation three years previously.

IV. Non-Union of Radius:—1.

V. Chronic Cholecystitis and Malfunction of Cholecystoduodenostomy:—1.
VI. Recurrent Cases of Pilonidal Sinuses:—8.

Cases described above under I b.(2), IV, and V (cases number 6, 16 and 20 respectively in Table I), and the group of cases under VI are deserving of special mention:

Case 6.—*Broncho-pleural Fistula with Talc Granuloma:*

The patient was a 52-year-old white male who entered the hospital April 29, 1947, complaining of cough and dyspnea. Symptoms had developed a few weeks following right lower lobe pneumonia. A diagnosis of empyema was made on the basis of physical and X-ray findings and on April 30, 1947, a thoracotomy and open drainage from the empyema cavity was done by Dr. Wilson Weisel, Consultant in Thoracic Surgery. The empyema was extensive with total collapse of the lung. Three large rubber drains were inserted into the thoracotomy wound for drainage. Following this the patient developed a broncho-pleural fistula and a "frozen" lung. On August 12, 1947, decortication was done to permit free motion of the lung, a considerable portion of the pleura and scar and granulation tissue being removed. The involved bronchus was closed with interrupted sutures of 000 black silk and the wound was closed using a muscle flap to fill the cavity defect. The fistula remained closed and the wound healed well. The surgical specimen consisted of pleura and granulation tissue removed from the region of the involved bronchus. The removed tissue microscopically showed a marked proliferation of fibrous tissue with groups of lymphocytes, plasma cells and eosinophilic cells, with occasional foreign body giant cells which were seen engulfing small refractile crystals which were birefringent with the polarizing lens.

Case 16.—*Non-Union of Fracture of Right Radius with Talc Granuloma:*

The patient was a 23-year-old white male who sustained a simple fracture of the right radius September 28, 1946. An attempted closed reduction was unsuccessful and therefore an open reduction was performed on October 3, 1946, by Dr. P. Collopy, Consultant in Orthopedic Surgery, with insertion of a metal plate and screws. The operative wound healed well, and the patient was discharged with his arm in a plaster cast. When he returned to the Out-Patient Department nine weeks after surgery for follow-up treatment, it was found that the wound had partially broken down and there was a moderate amount of granulation tissue and a seropurulent exudate at the wound site. X-ray at that time reported "only minimal new bone formation at the fracture site." The wound failed to heal under conservative treatment which included a regime of penicillin and sulfadiazine. On March 4, 1947, five months after the initial operation, the plate, screws and fibrous tissue from the site of non-union were removed, and the fragments were immobilized by means of Kirschner wires and a plaster cast. The surgical specimen showed fragments of bone encased in fibrous tissue. In addition there was an inflammatory infiltrate and an amorphous crystalline double refractory material, identical with talc crystals, enclosed in giant cells. The wound healed by first intention and three weeks later the patient was again operated, at which time a bone graft was applied to the site of non-union. An intermedullary as well as an onlay graft was used in order to correct a one-inch defect of the radius. The wound healed postoperatively without complication.

Case 20.—*Cholecystitis, and Non-Functioning Cholecystoduodenostomy with Talc Granuloma:*

This patient was a 45-year-old white male who entered the hospital July 13, 1946, because of an incisional hernia at the site of a previous laparotomy for gallbladder disease. He gave a history of having had a cholecystoduodenostomy in 1937, and an exploratory laparotomy in 1945 because of persistent biliary tract symptoms. At the time of his second operation (done in an overseas army hospital) the surgeon noted a contracted gallbladder and a greatly distended common duct which was explored and drained. No stones were present, and there was no apparent blockage of the common duct. The reason for the original cholecystoduodenostomy is unknown. On admission to this hospital it was

TABLE I.—*Summary of Talc Granuloma Cases*

Case No.	Initial Diagnosis	Initial Operation	Complication—Reoperated For	Operation	Pathologic Lesion	No. Times Initial Lesion Re-operated	No. Specimens Submitted	Results
1.	Tuberculous Empyema	Thoracotomy	Persistent drainage from operative wound.	Revision of Wound.	Talc granuloma in excised tissue.	1	1	Healed.
2.	Pulmonary Tuberculosis.	Thoracoplasty	Persistent drainage from operative wound.	Revision of Wound.	Talc granuloma in excised tissue.	2	2	Continued granulation—needs further revision.
3.	Pulmonary Tuberculosis.	Thoracotomy; Thoracoplasty	Persistent drainage from operative wound.	Revision of Wound.	Talc granuloma in excised tissue.	2	2	Healed.
4.	Pulmonary Tuberculosis.	Thoracoplasty	Persistent drainage from operative wound.	Revision of Wound.	Talc granuloma in excised tissue.	2	1	Healed
5.	Pulmonary Tuberculosis.	Phreniclasia	Granuloma of operative wound.	Excision of granuloma.	Talc granuloma in excised tissue.	1	1	Healed.
6.	Empyema (Post Pneumonic)	Thoracotomy	Broncho - pleural fistula. Persistent drainage from operative wound.	Decortication and Closure Broncho-pleural Fistula.	Talc granuloma in excised tissue.	1	1	Healed.
7.	Empyema (following ruptured Amebic Abscess)	Thoracotomy	Wound breakdown with chronic drainage from operative wound.	Revision of Wound.	Talc granuloma in excised tissue.	4	1	Healed.
8.	Rectal Fistula	Excision of Fistula.	Failure to heal and continued drainage of fistula.	Excision of Fistula.	Talc granuloma in excised fistulous tract.	1	1	Healed.
9.	Para-rectal Sinus	Incision and Drainage.	Continued drainage from sinus.	Excision of sinus.	Talc granuloma in excised sinus.	4	2	Healed.
10.	Ruptured Appendix	Appendectomy	Fecal Fistula	Biopsy of fistulous tract.	Talc granuloma in excised fistulous tract.	1	1	Fistula failed to heal. (Died)

TABLE I.—*Summary of Talc Granuloma Cases*

Case No.	Initial Diagnosis	Initial Operation	Complication—Reoperated For	Operation	Pathologic Lesion	No. Times Initial Lesion Re-operated	No. Specimens Submitted	Results
11.	Ruptured Appendix	Appendectomy	Fecal Fistula	Excision of fistula and closure of bowel.	Talc granuloma in excised fistulous tract.	1	1	Healed.
12.	Shell fragment wound.	Debridement of wound and secondary closure.	Chronic draining lumbar sinus.	Excision of sinus.	Talc granuloma in excised sinus.	1	1	Healed.
13.	Tuberculosis of kidney.	Nephrectomy	Chronic draining lumbar sinus.	Excision of sinus.	Talc granuloma in excised sinus.	1	1	Healed.
14.	Peripheral Vascular Disease.	Lumbar Sympathectomy.	Chronic draining lumbar sinus.	Excision of sinus.	Talc granuloma in excised sinus.	3	2	Failed to heal after 7 months. (Died of intestinal carcinoma.)
15.	Osteomyelitis of sacrum with draining sinus of left flank.	Curettement of sacrum, sequestrectomy, and excision of sinus.	Chronic draining lumbar sinus.	Excision of sinus.	Granulation tissue in excised sinus tract.	3	1	Failed to heal.
16.	Fracture Right Radius.	Open Reduction and Plating.	Non-union right radius.	Removal of plate and curettement. Bone graft.	Fibrous talc granuloma at site of non-union.	2	1	Healed.
17.	Gunshot wound of mandible.	Surgical treatment gunshot wound.	Tumor mass of mandible.	Excision of tumor.	Fibrous talc granuloma.	1	1	Cured.
18.	Angioma, right index finger.	Partial removal of angioma.	Progressing tumor mass right index finger.	Excision of tumor mass.	Fibrous talc granuloma.	1	1	Healed well.
19.	Right Inguinal Hernia.	Herniorrhaphy	Tumor mass right groin.	Excision of tumor.	Talc granuloma and organized hematoma.	1	1	Cured.
20.	Gall Bladder Disease	Cholecystoduodenostomy.	Chronic Cholangitis.	Common duct drainage. Cholecystectomy.	Chronic talc granuloma at site of Cholecystoduodenal anastomosis.	1	1	Healed (Symptoms alleviated.)

TABLE I.—*Summary of Talc Granuloma Cases*

Case No.	Initial Diagnosis	Initial Operation	Complication—Reoperated For	Operation	Pathologic Lesion	No. Times Initial Lesion Re-operated	No. Specimens Submitted	Results
21.	Carcinoma of Bowel.	Exploratory Laparotomy and resection of tumor.	Intestinal Obstruction and Fecal Fistula.	Repeated Laparotomies for intestinal obstruction and fecal fistula.	Talc granuloma of excised gangrenous bowel.	14	1	Wound never healed. (Patient died.)
22.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	1	1	Healed.
23.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	1	1	Healed.
24.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	10	1	Wound granulating and still not quite healed at discharge.
25.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	3	1	Wound broke down and finally healed slowly by granulation.
26.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	3	1	Healed.
27.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	3	1	Wound granulating and still not completely healed at discharge.
28.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	1	1	Healed.
29.	Pilonidal Sinus.	Excision of sinus.	Recurrent Pilonidal Sinus.	Excision of sinus.	Talc granuloma in excised tissue.	1	1	Healed.
29						71	33	— Total

noted that he had an icteric tinge to his skin and the icterus index was 22. The preoperative diagnosis at this hospital was chronic cholangitis based on the history of recurrent bouts of jaundice, chills and fever following cholecystoduodenostomy. Laparotomy was performed on July 30, 1946, by Dr. F. Raine, Senior Consultant in Surgery. Since cholecystogram revealed patency of the common duct, the anastomosis from the duodenum was taken down and the gall bladder was removed. Postoperatively, the patient had a stormy course with exacerbations and remissions of his cholangitis, but succeeding attacks

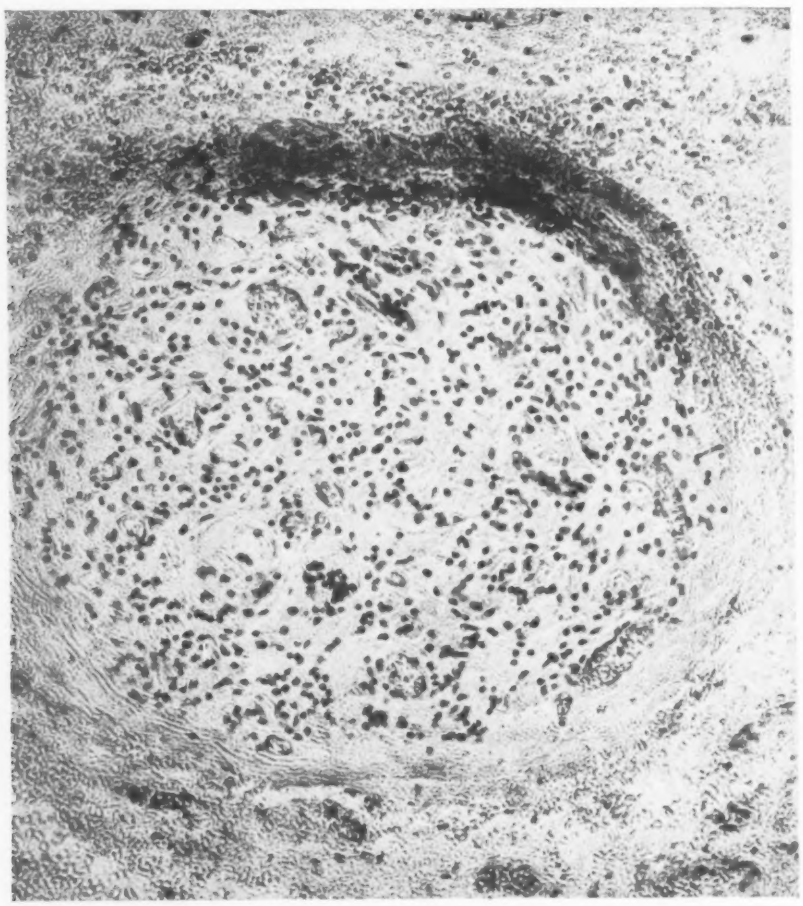

FIG. 1A.—(Case 20) Cholecystitis showing talc granuloma in wall of gallbladder at site of duodenal anastomosis (low power field).

were decreasingly severe and his icterus index gradually returned to normal. The microscopic examination of the gallbladder showed the mucosa to be normal but the wall showed round cell infiltration in the submucosal area and within the muscularis a large area was found to be surrounded by fibrous tissue, in which there were epithelioid cells and giant cells, some of which engulfed foreign particles which were identified under the polarizing microscope as talc crystals (Fig. 1a and 1b).

Talc Granuloma in Recurrent Pilonidal Sinuses. A special study was made of pilonidal sinuses. Since they are notably prone to recur, the thought was

entertained that talc might be responsible for these recurrences. There was a total 58 pilonidal specimens, of which 37 were primary and 21 were recurrent. Talc crystals were not found in any of the primary cases. In eight (38 per cent) of the 21 recurrent cases, talc was found. However, in all recurrent cases, remnants of epithelial cyst or sinus could be demonstrated. Thus it could be established that talc was not the primary cause for recurrence of a pilonidal sinus. The possibility that the talc crystals acted as an irritant to the lesion causing symptoms necessitating another operation cannot be excluded.

FIG. 1B.—(Case 20) Same as 1A under polarized light, showing talc crystals within macrophages and giant cells (low power field).

DISCUSSION

From our study, no support can be given for or against the previously mentioned dispute as to whether talc alone is innocuous without associated trauma. A large per cent of talc granulomata were found in thoracic (thoracoplasty and thoracotomy) cases. There were 12 specimens from thoracic cases in this series which had been diagnosed previously as non-specific inflammatory granulomas. Nine of these were found to be talc granulomas. The multiple stage procedures employed and the use of drains and frequent dressings

required in these cases afford repeated trauma as well as increased opportunity for talc implantation.

We believe that Case 6 is the first case of talc granuloma in a bronchopleural fistula to be recorded. Intraabdominal fistulae due to talcum powder have been repeatedly reported, and this has also been observed in experimental animals.[9, 10] In our case it cannot be stated how much of the responsibility talc must bear as the cause of the fistula, but at least it is a contributing factor to prevention of spontaneous closure of the sinus.

In the case of non-union of the radius (Case 16), it cannot be proved that talc alone was the cause of non-union. However, this was a clean case of elective surgery. The operative wound was healed at the time the patient was discharged. It subsequently broke down and continued to drain and would not respond to conservative therapy. This clinical picture of wound breakdown after primary healing, with the formation of a draining sinus that failed to heal on the usual regime of heat, rest, elevation, and antibiotics, is characteristic of talc granuloma. In addition, the microscopic evidence of typical talc granuloma in the fibrous tissue from the site of non-union indicates that talc in this case was the cause of non-union. The fact that primary healing rapidly occurred subsequent to the removal of the plate and fibrous tissue containing the talc, plus the fact that there is no other reasonable explanation for the failure of healing after initial plating, adds strength to the argument for talc as the etiologic agent here. We have found no previous reported case of non-union of a fracture due to interference of healing by talc.

In the case of gallbladder disease (Case 20), the introduction of talc into the wound at the time of initial surgery resulted in prolonged morbidity of the patient. The cause for the patient's original operation is not known. Nevertheless there was interference with function of the cholecystoduodenostomy as is evidenced by the observation of the surgeon at the time of the second operation for choledochotomy and drainage. He noted that the common duct was greatly distended and that the gallbladder was markedly contracted and apparently not functioning as a channel for the transport of bile to the duodenum. The talc in this case was not merely covered over with serosal cells so as to produce nodules on the peritoneal surface, as is usually the case, but was actually found in the wall of the gallbladder in the submucosal area and within the muscularis. The crystals undoubtedly were placed there when the cholecystoduodenostomy was performed. We feel justified in thus assuming that the gallbladder disease was due to talc. This was, in fact, a talc cholecystitis. We have found no similar case recorded in the literature.

There is a marked difference of opinion as to the incidence of talc granuloma. Fienberg[4] in 1937 reported two cases and stated that in a review of 30,000 specimens he had found a total of but five cases. Saxen and Tuovinen[16] in 1947 also report a low incidence, having found but six cases in 5,241 specimens. German[5] on the other hand, as mentioned above, reported 50 cases of talc granuloma, and stated that serial sections through the omentum of patients undergoing abdominal surgery for the second time would almost always contain talc. We found 33 cases of talc granuloma in a consecutive series of 1,912

surgical specimens. This would indicate that 1.7 per cent of the consecutive surgical procedures that were done were necessitated entirely or in part by talc. Actually, however, the figure is probably even higher than this, since a great number of wound granulomas and sinuses that are excised, many of which may contain talc, never reach the pathological laboratory. As an example, one patient had a chronic draining sinus excised on four different occasions and only one specimen was sent to the pathological laboratory, this specimen being a talc lesion. It is interesting to note (Table I) that of the 29 patients from whom these 33 specimens were obtained, 16 patients had one re-operation of the talc lesion concerned, whereas 13 patients (44.8 per cent) were reoperated two or more times, one patient having ten and another fourteen re-operations. Theoretically the talc could have been inserted into the wound at the time of the initial surgery or at any of the subsequent operations prior to the last one. It is further significant to note that these 29 patients underwent a total of 71 operations subsequent to their 29 initial procedures.

CONCLUSIONS

1. In a series of 1,912 routine consecutive surgical specimens, talc granuloma was found in 33.

2. Of the consecutive surgical procedures from which the above specimens were obtained, 1.7 per cent of the operations performed were necessitated in whole or in part by talc.

3. Draining sinuses following chest surgery were found to be frequently complicated by talc granuloma. In specimens from nine out of the twelve chest cases examined, talc was considered to be a major factor in the production and persistence of these sinuses.

4. To the reported cases of talc granuloma, one each of broncho-pleural fistula, failure of function of a cholecystoduodenostomy, and non-union of a fracture of the radius, is added.

5. In eight of 21 cases (38 per cent) of recurrent pilonidal sinuses, talc reaction was noted. Since in each case residuals of the sinus tract could be demonstrated, recurrence of the sinus could not be primarily attributed to talc. The talc may, however, act as an irritant necessitating revision.

6. Excision of the granuloma with the talc with resultant healing of the wound was accomplished in 21 out of the 29 cases of talc granuloma.

7. The inadvisability of the use of talc as a dusting powder is again emphasized.

Note: Photomicrographs were kindly prepared by Mr. Leo Massopust of Marquette University School of Medicine.

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COMPLICATIONS OF GASTRO-INTESTINAL INTUBATION*

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GASTRO-INTESTINAL INTUBATION is one of the most important of the non-operative procedures available for the hospital care of patients. There is hardly any portion of the alimentary tract that has not been aspirated, deflated, fed or treated by rubber tubes. That such extensive threading of tubes through 32 feet of undulating, flexible, twisting intestine has encountered so few accidents is even more phenomenal than the occasional interesting account of such mishaps. Case reports of accidents resulting from gastro-intestinal intubation have been intermittently creeping into the literature. Some are merely medical curiosities; others have recorded tragedy for patients. Although the subject merits a collective review, it is believed that no article devoted exclusively to the complications of gastro-intestinal intubation has been previously published.

It is emphasized at the outset that disturbances in fluid and electrolyte balance induced by the indiscriminate use of gastro-intestinal suction are by far the most frequent and dangerous complications. One has only to measure the 24-hour volume and chloride content of secretions aspirated by a stomach tube to appreciate how quickly dehydration, hypochloremia and alkalosis may develop in a patient in whom these substances are not replaced. This physiologic phase of the subject has been amply covered by others as have the indications and contraindications of gastro-intestinal intubation. This paper is devoted entirely to the less discussed complications due to the mechanical presence of tubes in the intestinal tract.

Four case reports from the author's personal observation are submitted. The first two are knotting respectively of a Levine and Miller-Abbott tube in the stomach, the third a fatal hemorrhage from prolonged contact of a Miller-Abbott tube with esophageal varices, and the fourth a perforation of a gastric carcinoma from an indwelling Levine tube.

The complications of gastro-intestinal intubation may be classified as follows:

I. SINUSITIS AND OTITIS MEDIA

An inlying rubber tube of long standing in the nasal passage can create an inflammatory response of the nasal mucous membrane. Sinusitis then develops from infection coupled with improper drainage of the sinuses. For similar reasons otitis media is a not infrequent complication of indwelling nasal tubes in children. Apparently of no serious import judging from lack of emphasis in the literature, these complications are mentioned more for sake of completeness. It is obvious, however, that it is undesirable to use indwelling nasal tubes in patients with head colds or acute sinusitis.

* Received for publication, September, 1948.

II. ESOPHAGEAL STRICTURE

Pathologists frequently observe inflammatory reaction and erosions at autopsy in the esophagi of subjects who were submitted to prolonged gastric intubation before death. Vinson[1] reports three cases of benign cicatricial stricture of the esophagus in patients submitted to continuous intubation for periods varying from two to four weeks. All responded favorably to repeated esophageal dilatations. Vinson cites this as a new cause for esophageal stricture which may crop up in the future and for which investigation should be made in patients having dysphagia following prolonged gastric intubation.

III. LARYNGEAL OBSTRUCTION

This is perhaps the most feared and insidious complication of gastrointestinal intubation. One cannot read the case reports without forever after being on the alert for the premonitory symptoms. Nineteen case reports are available of laryngeal obstruction caused by the presence of inlying tubes in the esophagus. Of these, 15 required tracheotomy and four died. The ages of these patients varied from five to 62 years. The Miller-Abbott, Levine, and Jute tubes were implicated.

The lessons to learn from the ten case reports of Iglauer & Molt[2] are that the obstructions can be insidious or rapid and that invariably they occur days *after* the tubes have been removed. In their series tubes remained in the stomach from 6 to 20 days, the average being 8½ days. Tracheotomies were performed from 5 to 30 days following removal of tubes from the esophagus. In one of the three cases reported by Holinger and Loeb,[3] a tracheotomy was required seven weeks after the withdrawal of a Levine tube which had been in place only four days. At the time of publication of their article all but one of the tracheotomies performed by Iglauer & Molt were permanent. Others reporting cases of laryngeal obstruction are Wangensteen[4] (two cases), Kaufman *et al.*,[5] Mahon,[6] Hippenmeier,[7] and Soubiron *et al.*[8] (each one case).

The essential findings in these cases were those of pressure necrosis of the esophagus near its attachment to the body of the cricoid cartilage. At this point the thin wall of the esophagus affords very little cushion between the mucous membrane and the cartilage. Perichondritis and ulceration of the mucous membrane of the adjacent cricoid cartilage follows with consequent acute subglottic stenosis of the larynx.

The warning symptoms of impending laryngeal obstruction in these cases are dyspnea, dysphagia, hoarseness, blood streak sputum, and croupy cough. The onset of dyspnea is an ominous sign, for this develops gradually over a period of days. Less frequently does dyspnea develop rapidly before tracheotomy is required. Kaufman *et al.* recommend daily mirror inspection of the larynx for inflammation or edema and withdrawal of the tube if the patient develops dysphagia or hoarseness.

IV. KNOTTING OF THE TUBE

Many radiologists have observed potential knotting of a tube in the stomach, but in its withdrawal the knot is usually disentangled. Removal from

the stomach via the esophagus of a knotted tube doubtless has occurred more than the reports would indicate. The reports of Billings,[9] Boles,[10] Niles,[11] Golob,[12] Paviot & Levrat,[13] Francesco,[14] and Martini *et al*[15] make a collection of seven cases of knotting of tubes. Each reports a case of knotting of a metal tipped Rehfus type tube in the procedure of biliary drainage. All but one of these tubes knotted in the stomach and in each case the incident was attributed to gastric hypermotility.

In the case of Billings a Rehfuss tube was passed without incident for proposed biliary drainage. After waiting 30 minutes for passage into the duodenum, the patient suddenly became dyspneic and attempted to remove the tube herself, but encountered difficulty passing the cardiac orifice. By having the patient swallow water her physician was able to draw the tube past the cardiac orifice and slowly by resistant jerky efforts to bring it up the esophagus. Two separate single knots were present starting one inch from the metal tip. With the exception of Paviot & Levrat's case all tubes knotted in the stomach and were withdrawn in a similar resistant jerky manner without any apparent after ill-effect on the patient.

The most unusual report is that of Paviot and Levrat from France. At 9:00 P.M. a nearly new metal tipped Einhorn tube was passed for biliary drainage without incident on a 37-year-old male having cholelithiasis. During the night 80 cc. of bile had drained from the duodenum. The next morning after giving atropine and magnesium sulfate the patient became nauseated and attempted emesis. Only 10 cm. of the tube could be withdrawn and this was apparently from stretching of the rubber in an otherwise immovable tube. Radiologic examination disclosed a double complex knot of the tube in the duodenum caught against the pyloric sphincter. Atropine and bromides failed to permit withdrawal. The following day the tube was divided with scissors as far down the pharynx as possible. Forty-eight hours later the entire tube along with the double knot measuring 3 x 5 cms. passed spontaneously at the anus. These authors attributed this accident to the prolonged presence of the tube in the duodenum. Whether the tube might not have tied itself in the stomach and then passed through the pyloric sphincter is not mentioned.

Two additional instances of knotting of tubes within the stomach are given from the author's experience while surgical resident at the Episcopal Hospital in Philadelphia.

Case 1.—W. J., 38-year-old colored male had an ileocolostomy and exteriorization of a gangrenous irreducible ileocecal intussusception on November 17, 1947. Postoperatively a Levine tube was passed. It remained in place 5 days and was then withdrawn because of ineffective drainage. The interne was surprised to find the tube tightly tied in a single knot one inch from its tip.

Case 2.—J. S., male, age 56, had symptoms of intermittent large bowel obstruction of 5 days duration. On December 1, 1947, a Miller-Abbott tube was passed at 9:00 P.M. The following morning after drainage of 240 cc. of gastric contents, the patient passed flatus and a formed stool. It was decided to remove the tube and give barium by mouth. The clamp on the balloon side of the tube was removed in the routine manner. The

patient asked to withdraw the tube himself and in so doing encountered considerable jerky resistance. After moderate effort the tube and knot came out the nose (Fig. 1). Four inches from its tip the tube was tied in a single loop knot. The balloon was empty and

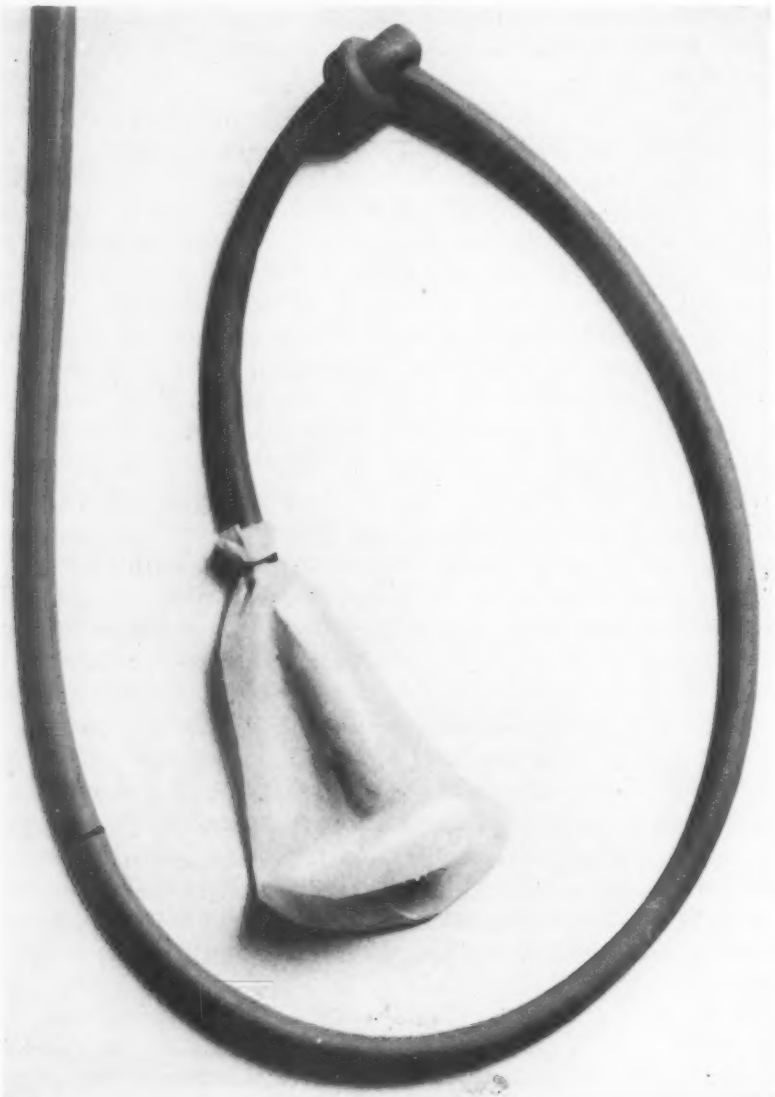

FIG. 1.—Photograph of Miller-Abbott tube knotted 4 inches from its tip. It was withdrawn by a patient after being in his stomach 12 hours.

unruptured which suggested that the knot must have been tightly drawn at the time of removal of the tube and just after the escape of air from the balloon. The patient had no ill effects from the incident.

V. RUPTURE OF ESOPHAGEAL VARICES

Schindler[16] lists esophageal varices among the absolute contraindications for gastroscopy, fearing hemorrhage from its use. It would seem that for parallel reasons esophagogastric intubation would be contraindicated in any patient with cirrhosis of the liver suspected of having esophageal varices. A review of the Index Medicus since 1912 has failed to unearth a single article or case report devoted to rupture of esophageal varix from a tube inlying in the esophagus. The following case report should therefore be interesting, if indeed, this is the first such case report.

Case 3.—H. S., 63-year-old male was admitted to the medical service of Episcopal Hospital, Philadelphia, on January 22, 1947, with acute onset of knife like precordial pain of 15 minutes duration, orthopnea, and abdominal distention allegedly of 4 days duration. He was a known alcoholic. His cardiac failure responded well to digitalization. The abdomen was distended but not tender and presented a shifting dullness. Radiologic survey of the abdomen revealed distention of the stomach and small intestine. Some confusion existed as to the cause of the patient's abdominal distention. Believing there existed a combination of ascites and intestinal obstruction the resident passed a Levine tube into the stomach for continuous suction. On January 23rd a Miller-Abbott tube was passed and on January 24th radiologic examination disclosed its tip well into the small intestine with considerable diminution in the distention. After the removal of 4 liters of serous fluid with specific gravity of 1.012 by paracentisis abdominis, the liver edge was readily palpated at the level of the navel. It was firm and coarsely nodular. The Miller-Abbott tube remained in place to prevent recurrence of intestinal distention. On January 29th, after 7 days of intubation, he vomited about a liter of bright red blood followed by the passage of bloody stool a few hours later. In spite of repeated transfusions and other supportive measures, the patient died of exsanguination on January 31st, 36 hours after the onset of hemorrhage.

At autopsy about 3 liters of straw colored fluid was free in the peritoneal cavity. The liver weighed 1850 Gm., was studded on its surface with brown nodules as great as 2.5 cms. in diameter. This nodularity continued throughout the parenchyma as circumscribed tumor masses, some of which were soft and others almost cystic or necrotic. Very little normal liver tissue could be demonstrated. The spleen weighed 240 Gm. The entire gastro-intestinal tract was filled with clotted fresh blood. No obstruction was present. The esophagus was grossly inflamed and presented numerous varicosities of the distal third. There was frank ulceration and necrosis of the mucosa overlying at least 2 of these veins. It appeared that this had been the source of the bleeding.

Histologic examination of the liver tumor performed by the Department of Pathology at Temple University Hospital confirmed the impression that this was a primary hepatoma superimposed on a long standing cirrhosis of the liver. Microscopic sections of the esophagus (Fig. 2 and 3) demonstrated varicosities with deep ulceration of the mucous membrane.

COMMENT: While it cannot be proved that this hemorrhage from esophageal varices might not have occurred spontaneously without the presence of an indwelling tube, the knowledge that a Miller-Abbott tube was in contact for six days with varices of the esophagus and the demonstration of esophagitis and ulceration at autopsy appear to bear more than coincidental relationship to the hemorrhage.

VI. RUPTURED VISCUS

It is a surgical principle to obviate pressure necrosis and perforation of such structures as blood vessels, mesentery and serosa of gut by studiously avoiding prolonged contact of these structures with hard rubber drains and tubes. Analogous to this it might be implied that similar precaution should be exercised in regard to intestinal intubation, at least with respect to diseased gut. A wealth of experience with intubation under all circumstances had shown little cause for concern until the revealing papers of Mahon,[6] Eliason and Welty,[17] Berger and Achs,[18] and Holinger and Loeb.[3] Their cases are here abstracted

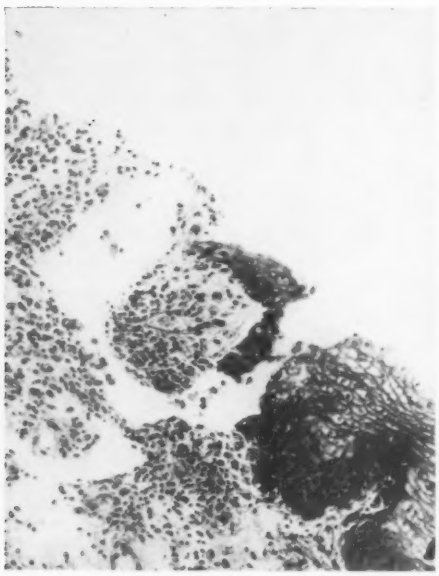

FIG. 2

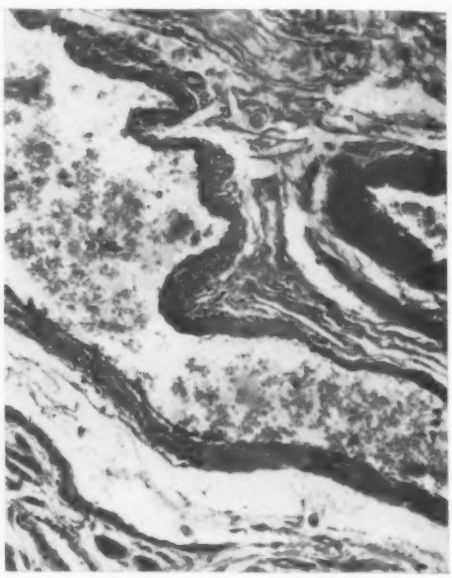

FIG. 3

FIG. 2.—Photomicrograph of esophagus of Case 3, showing stratified squamous epithelium undergoing necrosis with invasion by lymphocytes and neutrophils. x 100.
FIG. 3.—Photomicrograph of esophagus of Case 3. This shows greatly dilated and blood filled veins in the submucosa of a patient with esophageal varices. x 100.

along with an additional one by the author to serve as a warning that perforated gut can occur from the presence of inlying tubes. That each case is different suggests the wide possibilities of this accident.

The first case report of ruptured stomach attributed to the presence of an inlying gastric tube is that of Mahon. A female had 18 inches of gangrenous ileum resected with end-to-side anastomosis of ileum to ascending colon. A Levine tube was passed into the stomach for aspiration and remained in place nine days. Two days following removal of the tube she suddenly developed laryngeal obstruction necessitating a tracheotomy. Death occurred in 10 hours. At autopsy massive atelectasis of two lobes of the lung secondary to complete inflammatory occlusion of the larynx was seen along with four areas of necrosis

on the anterior wall of the stomach just above the greater curvature. Perforation of the stomach had occurred through two of these areas presumably by pressure necrosis. The cause of death was due to peritonitis and massive atelectasis.

The second in this series is a case report by Eliason and Welty suggesting the possibility of perforated esophagus from intubation. Their 44-year-old female patient was intubated by a Levine tube for 36 hours following a resection of strangulated small bowel. The tube was then removed because of respiratory distress. Repeated vomiting of coffee ground material followed removal of the tube. At autopsy a rupture of the anterior wall of the distal end of the esophagus was found. The adjacent mediastinal tissues were deeply stained with partially digested blood. These authors mention that the role which the Levine tube may have played is uncertain. A third and similar case was reported by Holinger and Loeb. Their 57-year-old female patient eviscerated eight days after a gastroenterostomy for extensive carcinomatosis. Because the "stomach tube" was poorly tolerated by the patient it was removed and repeatedly reinserted during a period of 11 days. A final overzealous attempt to insert it resulted in a perforation of the esophagus with death from a mediastinal abscess.

The fourth in this series is the case reported by Berger and Achs. A 40-year-old female was admitted with small intestinal obstruction caused by an adhesion band at the ileum. Because the patient refused operation, a Miller-Abbott tube was passed. It migrated to the ileum to a point where it would not proceed further in spite of the fact that it was repeatedly withdrawn to the 18-inch mark over a period of 12 days. On the tenth day of intubation there was no drainage from the tube. On the 12th day of intubation a celiotomy disclosed the metal tip of the Miller-Abbott tube protruding through a perforation in the ileum just proximal to the obstructing band. The balloon was unruptured. The patient made an uneventful recovery after division of the band and closure of the perforation. This accident was attributed to pressure necrosis of a dilated, thin walled, and obstructed intestine caused by prolonged contact with the metal tip. The authors believed this to be the first report of rupture of small intestine from intubation.

The fifth in this series is case 4 reported by the author.

Case 4.—A. G., No. 8067, male, age 56, admitted to Hamot Hospital, Erie, Penna., on October 19, 1946, having been referred by Dr. Harold Ghering, of Edinboro, Pa. The patient had a two-weeks history of marked weight loss, anorexia, and vomiting. Physical examination was essentially negative aside from presence of marked cachexia. Peritoneoscopy performed on October 21st disclosed pyloric carcinoma with liver metastasis. Because of obstructive symptoms a gastroenterostomy was decided upon. The patient's stomach was prepared for two days with continuous Levine tube suction and gentle lavage with normal saline solution. On October 23rd Dr. Orel Chaffee performed a celiotomy through a left para-median incision. The tumor previously visualized by peritoneoscopy was found encircling the distal third of the stomach, Fig. 4. On the anterior surface of the stomach through the midst of the tumor there was a perforation about 8 mm. in diameter through which the tip of a Levine tube was just protruding into the peri-

toneal cavity. A plastic exudate encircled the perforation. There was almost no fluid in the peritoneal cavity and very little inflammatory reaction. The stomach which had been frequently flushed and continuously aspirated for 48 hours in preparation for gastric surgery was now clean, empty, and of normal size. The tube was withdrawn 4 inches by the anesthetist and the perforation in the tumor closed by a purse string suture of No. 0 chromic catgut. An anterior gastroenterostomy was then performed. The patient made an uneventful recovery and at the time of hospital discharge on November 7th had gained 5 pounds and was able to ingest a soft diet without distress. According to Doctor Ghering his condition continued at home unchanged until November 30, 1946, when he died suddenly of a coronary infarction.

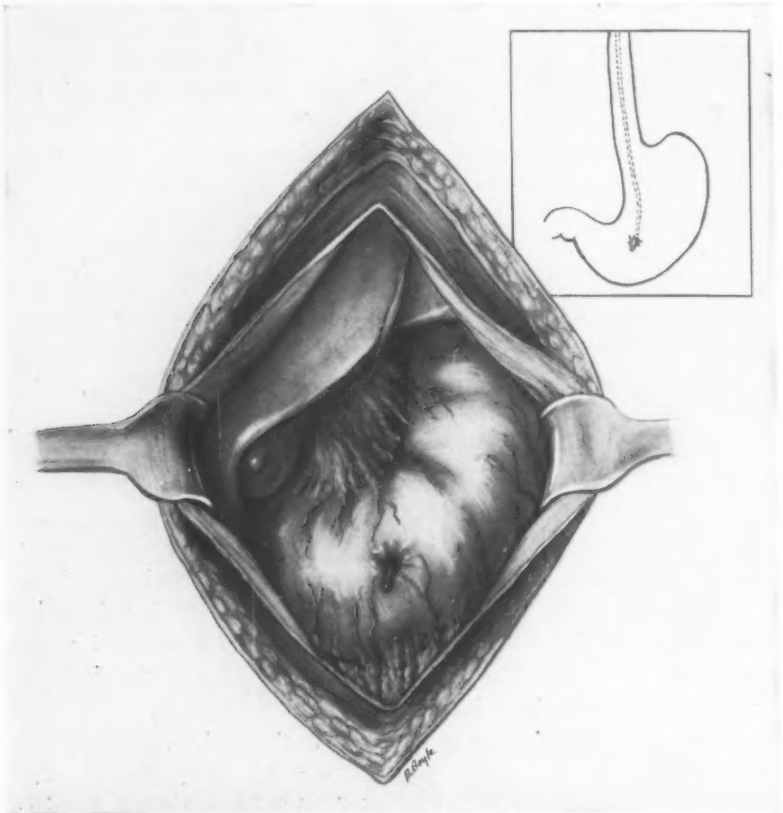

FIG. 4.—Case 4: Artist's concept of Levine tube perforating stomach at area of carcinomatous degeneration. Inset at right is a schematic drawing of the tube in relation to the stomach.

COMMENT: Here again the perforation is attributed to pressure necrosis of the stomach by an inlying tube. In this case it occurred in only two days of intubation because this was a carcinomatous stomach. A rule to grow out of these experiences is the following: "Make sure that the tip of the tube changes its position in relation to the gut daily." This can best be done by having the patient either swallow more tubing or withdraw a portion each day.

Bisgard and Overmiller[19] collected 217 reported cases of spontaneous rupture of the stomach. Glassman[20] in his classical review of spontaneous perforation of the stomach warns that very slight trauma may cause perforation of a diseased stomach wall. Strassman[21] and Key[22] have each reported a case of spontaneous rupture of the stomach during gastric lavage. These mishaps were doubtless due to the volume or force of fluid used in the diseased stomach and not to the presence of a tube. As such they would be classified along with the remarkable case reports of Lemmon and Paschal[23] and Murdfield.[24] In their patients the stomachs ruptured after being filled with large quantities of beer or other fluids followed by ingestion of sodium bicarbonate.

VII. INABILITY TO WITHDRAW THE BALLOON TIPPED TUBE

It is entirely possible that a situation could exist where the balloon of a Miller-Abbott tube could not be deflated. Patency of the air channel of the tube and free communication with the balloon should be determined daily. This may be done by aspirating all air out of the balloon after removing the clamp on the air outlet tube. In a dry syringe, about 15 to 20 cc. of air may then be injected into the balloon. If there is a free communication of the air channel the plunger will be forced back into the syringe by the elasticity of the balloon. If there is doubt about whether the balloon is deflated or any resistance encountered in withdrawing the tube, one should never forcibly pull on the tube. A roentgenogram will immediately determine whether or not the balloon is collapsed.

Wangensteen[25] cites the case of an hour glass deformity of the balloon occurring at the ileocecal junction. The tube could not be withdrawn nor could the portion of the balloon beyond the ileocecal sphincter be deflated. Finally the balloon spontaneously ruptured permitting withdrawal. A tentative diagnosis of stricture at the terminal ileum was not substantiated at exploration.

Allen and Welch[26] state that they have had Miller-Abbott tubes descend to the lower small intestine and then found that the balloon did not deflate. Their suggestion for handling this complication is to perform an early laparotomy and to puncture the balloon through the intestinal wall with a needle.

Harris and Gordon[27] in writing about their mercury filled balloon cite one experience where the balloon could not be withdrawn after it had passed beyond the ileocecal valve. Persistent attempts to pull the bag through the valve resulted in a tear of the bowel with formation of a localized abscess. They now advise cutting the tube at the nares if the bag passes beyond the ileocecal valve. The entire tube then is eliminated spontaneously at the anus. In their seven experiences of this sort the time taken for the tube to appear at the anus varied from 24 hours to 10 days. Attempts to obviate this with the Harris tube have now been made by reducing the length so that only four feet of the tube can pass into the intestine. They further stress that the position of the tube be determined by radiologic examination after it has passed the 3-foot mark.

VIII. BREAKAGE OF MERCURY FILLED BAG

Breakage of a mercury filled bag in the intestine has occurred to almost everyone who extensively uses the Harris or Cantor tube. No ill effects have been reported from this phenomenon.

SUMMARY

1. An attempt has been made to review all of the reported complications of gastro-intestinal intubation since the first one recorded in 1924. The total number is not great in proportion to the widespread use of intubation.

2. The following headings are the complications discussed:

I. Sinusitis and Otitis Media
II. Esophageal Stricture
III. Laryngeal Obstruction
IV. Knotting of the Tube
V. Rupture of Esophageal Varix
VI. Ruptured Viscus including esophagus, stomach, and small bowel
VII. Inability to withdraw Balloon Tipped Tube
VIII. Breakage of Mercury Filled Bag

3. Four original case reports are presented of knotting of the tube, perforation of a cancerous stomach, and rupture of esophageal varices.

4. Warning notes are sounded to avoid complications with gastrointestinal intubation as follows:

a) Remove tube if the patient presents a dyspnea, dysphagia, hoarseness, blood streak sputum, or croupy cough.
b) Position of the tip of the tube should be changed daily.
c) Nasal intubation should be avoided in patients with sinusitis and head colds.
d) The presence of esophageal varices is a contraindication to gastric intubation.
e) Remove the tube as soon as it has completed its mission.
f) Tubes with mercury bag should be followed by roentgen ray after the 3-foot mark has been reached to prevent them from passing beyond the ileocecal valve. In the event the bag passes the ileocecal valve, it must not be withdrawn, but rather permitted to pass spontaneously by anus.

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INADVERTENT GASTRO-ILEOSTOMY*

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FORTUNATELY, the surgical error of anastomosing the stomach to the ileum instead of to the jejunum is uncommon. Twenty-seven cases of gastro-ileostomy have been found recorded in the literature. The first was reported in 1915 by Martin and Carroll.[1] Mercur[2] in 1917 reported another and mentioned a case seen by Judd in 1912. A fourth was mentioned by Klein[3] in 1926. These last two cases were not reported in detail and are excluded. Nine cases were added by Rivers and Wilbur,[4] three by Kogut and Stein,[5] eight by Smith and Rivers,[6] three by Brown, Colvert and Brush,[7] and one by Bailey and Castleton.[8] Two others are excluded (Rivers and Wilbur) because they were actually gastrojejunostomies with jejuno-ileostomies, although the clinical syndromes produced were similar.

An interesting and constant feature about the reported instances of gastro-ileostomy is that the original operation was performed by some surgeon other than the one reporting the case. This might imply that many such cases are never reported and that this condition is not as rare as a review of the literature would indicate.

Twenty-two of the 24 cases previously reported in sufficient detail to include in this study were patients on whom a gastro-enterostomy was being done for peptic ulcer. In only two reported instances has this condition been associated with a partial gastrectomy. One of these was reported by Kogut and Stein[5] and the other by Smith and Rivers.[6] The case reported herewith is the third reported instance in which a partial gastric resection was done with an anastomosis between the stomach and the ileum. Of the three cases with gastro-ileostomy following partial or subtotal gastric resection, two were done for duodenal ulcer and one for carcinoma of the antrum of the stomach.

A brief summary of the reported cases of gastro-ileostomy is presented in Table I.

It is felt that the occurrence of a gastro-ileostomy following gastric resection is sufficiently rare to justify another report. Of particular interest in this case is the associated malrotation of the midgut, which was a large factor in causing this surgical error. None of the previously reported cases had such an associated condition to explain why the ileum was mistaken for the jejunum.

CASE REPORT

Miss N. P., Hosp. No. 16–314, a 38-year-old white nurse, was admitted to Salt Lake General Hospital on December 7, 1947, with complaints of diarrhea, severe weight loss and increasing weakness of 18 months' duration.

* Submitted for publication, February, 1949.

TABLE I.—*Summary of Reported Cases of Inadvertent Gastro-Ileostomy.*

Reported by	Age and Sex of Patient	Original Diagnosis and Operation	Duration of Gastro-ileostomy Before Reconstructive Surgery	Weight Loss Since Gastro-ileostomy in Pounds	Reconstructive Procedure	Result
1. Martin and Carroll 1915	26 F.	Gastric ulcer. Gastro-ileostomy	12 mos.	Yes, but amount not stated	Reconstruction of normal pathway	Good
2. Mercur 1917	38 F.	?Duodenal ulcer. Gastro-ileostomy	3 yrs.	Yes, but amount not stated	Reconstruction of normal pathway	Good
3. Rivers and Wilbur 1932	35 F.	Duodenal ulcer. Gastro-ileostomy	6 mos.	25	Partial gastrectomy with reconstruction	Good
4. Rivers and Wilbur 1932	44 M.	Gastric ulcer. Gastro-ileostomy with jejuno-ileostomy	4 yrs.	18	Reconstruction of normal pathway	Good
5. Rivers and Wilbur 1932	39 M.	Gastric ulcer. Gastro-ileostomy	20 mos.	45	Reconstruction of normal pathway	Good
6. Rivers and Wilbur 1932	44 F.	?Duodenal ulcer. Gastro-ileostomy	17 mos.	Not stated	Reconstruction with gastro-duodenostomy (plastic)	Good
7. Rivers and Wilbur 1932	31 M.	Duodenal ulcer. Gastro-ileostomy	14 mos.	50	Reconstruction of normal pathway	Unknown
8. Rivers and Wilbur 1932	43 F.	?Duodenal ulcer. Gastro-ileostomy	13 mos.	Not stated	Reconstruction of normal pathway	Good
9. Rivers and Wilbur 1932	35 F.	?Duodenal ulcer. Gastro-ileostomy	25 yrs.	30	Reconstruction of normal pathway	Good
10. Kogut and Stein	27 M.	Duodenal ulcer. Gastro-ileostomy	1 yr.	Not stated	Reconstruction after excising ulcers of stomach and ileum at anastomosis	Recurrent ulcer. Post gastro-enterostomy done later
11. Kogut and Stein	26 M.	Duodenal ulcer. Gastro-ileostomy	2 yrs.	Yes; great but number of pounds not stated	Partial gastrectomy	Good
12. Kogut and Stein	63 M.	Ca. of stomach. Partial gastrectomy	No reconstructive surgery	Not stated	None	Died several days postoperatively
13. Smith and Rivers 1943	35 F.	?Duodenal ulcer. Gastro-ileostomy	6 mos.	25	Reconstruction	Good
14. Smith and Rivers 1943	53 F.	Duodenal ulcer. Gastro-ileostomy	9 mos.	36	Reconstruction and P. G. J.	Good
15. Smith and Rivers 1943	37 M.	Duodenal ulcer. Gastro-ileostomy	3 yrs.	6 pounds in preceding 4 weeks	Reconstruction and pyloroplasty	Pain recurred

TABLE I.—(*Continued*)

Reported by	Age and Sex of Patient	Original Diagnosis and Operation	Duration of Gastro-ileostomy Before Reconstructive Surgery	Weight Loss Since Gastro-ileostomy in Pounds	Reconstructive Procedure	Result
16. Smith and Rivers 1943	56 M.	Duodenal ulcer. Gastro-ileostomy	8 yrs.	36	Reconstruction and pyloroplasty with temporary feeding jejunostomy and cholecystectomy	Good
17. Smith and Rivers 1943	61 M.	?Duodenal ulcer. Gastro-ileostomy	3 mos.	60	Reconstruction with gastro-jejunostomy	Good
18. Smith and Rivers 1943	53 M.	Duodenal ulcer. Gastro-ileostomy	23 yrs.	Yes (7 pounds in 3 months preceding)	Reconstruction	Good
19. Smith and Rivers 1943	34 M.	Duodenal ulcer. Gastro-ileostomy	2 yrs.	5	Partial gastrectomy	Good
20. Smith and Rivers 1943	58 M.	Duodenal ulcer. Partial gastrectomy with gastro-ileostomy	6 mos.	60	Reconstruction	Good
21. Brown, Colvert and Brush 1947	62 F.	Duodenal ulcer. Gastro-ileostomy	4 yrs.	28	Reconstruction	Good
22. Brown, Colvert and Brush 1947	39 M.	Duodenal ulcer. Gastro-ileostomy	2 yrs.	20	Partial gastrectomy	Good
23. Brown, Colvert and Brush 1947	64 M.	Duodenal ulcer. Gastro-ileostomy	7 yrs.	44	Not stated	Good
24. Bailey and Castleton (in press)	72 M.	Duodenal ulcer. Gastro-ileostomy	2 yrs.	30	Reconstruction of normal pathway	Good
25. Moretz	38 F.	Duodenal ulcer. Subtotal gastrectomy with gastro-ileostomy	18 mos.	101	Reconstruction after block resection of anastomosis	Good

Ten years prior to her admission, she had first noted occasional severe epigastric pain. This was not related to meals but was relieved by milk or cream and antacids. These pains became more frequent and more severe and later were relieved by eating.

Seven years before her admission, she had had an episode of fairly massive hemorrhage after an attack of severe epigastric pain associated with the passage of 10 tarry stools and weakness. Shortly thereafter an exploratory laparotomy was carried out by a competent surgeon. An anomaly was noted in the duodenal region. The duodenum extended straight downward into the jejunum without going behind the superior mesenteric vessels or becoming retroperitoneal. The lower part of the second and third portions of the duodenum had a well-developed mesentery from two to three inches long. A duodenal ulcer was demonstrated and "the ulcer-bearing area was inverted."

Following this operation she continued on a strict medical regimen with exacerbation of her symptoms when the diet was relaxed or when there was added emotional strain. She had occasional bouts of increased pain associated with tarry stools in 1945 and 1946.

While she was attending college she noted increased pain and tarry stools with each examination week.

In July, 1946, a subtotal gastrectomy was carried out by the same surgeon. He noted the presence of many dense adhesions throughout the abdomen and it was only after much difficult dissection that he was able to liberate the stomach and pylorus sufficiently to allow resection of approximately two-thirds of the stomach. There were so many adhesions present that it was not possible to trace the small bowel back to the duodenum or the ileocecal valve for positive identification. A loop of small intestine lying in the left upper quadrant was used in constructing the gastro-enterostomy.

The postoperative course was satisfactory except that on her third postoperative day a severe diarrhea developed which never entirely ceased. The number of defecations per day varied from two to twenty. The stools were frequently bulky with very foul odor and occasionally frothy. Undigested food particles were occasionally seen in the stool 45 minutes after being ingested. She progressively lost weight and strength in spite of added vitamins and liver injections. No abdominal pain similar to that experienced prior to surgery occurred. There were occasional "gas pains" and frequent crampy pains for a few minutes after the passage of feces. During the six months prior to her admission here, she was bedridden. Her weight had decreased from 191 pounds prior to gastrectomy to 100 pounds on her present admission to the Salt Lake General Hospital. Food intake had continued to be adequate for a normal person. There was occasional vomiting or eructation of fecal character.

Her past history was irrelevant except for (1) an appendectomy in 1920, complicated by disruption of the right-rectus incision (the wound was resutured and the patient was discharged after one month of hospitalization), and (2) small-bowel obstruction in 1936 requiring laparotomy with release of adhesions (no further significant difficulty with obstructive symptoms occurred).

Examination revealed a markedly emaciated, tall, intelligent woman who lay quietly in bed. She rolled her head from one side to the other on request but was barely able to lift her head from the pillow. She could hardly lift her knees from the bed and was unable to lift either entire lower extremity. Her temperature was 98.6 F., pulse 76, respiration 20, blood pressure 85/65, height 5 feet 9½ inches, weight 100 pounds.

Except for the extreme emaciation, abnormal physical findings were scarce. Her skin was loose and pale. Her tongue was bright red, with enlarged papillae. There were three well-healed abdominal incisions: one in the lower midline, one in right rectus and one in left upper rectus. No solid organs or masses were palpable within the abdomen. Very slight tenderness was present in the left lower quadrant.

Slight edema was present in the left lower extremity chiefly at the ankle and upper thigh. Her marked generalized muscular weakness was compatible with her extreme emaciation.

Laboratory Findings:

Blood: Red blood cells 4.17 million; hemoglobin 12.5 gm.; hematocrit 38; icterus index 5; uncorrected sedimentation rate 2.0; MCV 91; MCH 30; white blood cells 5,050 with differential of 48/P, 40/L, 5/E, 5/M, 2/juveniles; blood chemistry: BUN 9.5; sugar 83; carbon dioxide 58; Pl. Cl. 600; total protein 4.0 (albumin 2.0, globulin 2.0); calcium 9.2; phosphorus 4.8; alkaline phosphorus 3.2 B.U.; uric acid 4.6.

Stool: Guaiac negative. Soft yellow with undigested food but without abnormal particles of fat; no parasites; 17.6 per cent of feces were solids; 11.2 per cent of feces were total lipids; 2.54 per cent of feces were fatty acids; 63.6 per cent of solids were total lipids; 14.4 per cent of solids were fatty acids; 22.7 per cent of total lipids were fatty acids.

Urine: Pale yellow—specific gravity 1.010, Ph 6, sugar 0, albumin 0. Microscopic: normal.

Gastric analysis revealed no free acid in the fasting specimen or after histamine. There were seven units of total acid in the fasting specimen and 20 units 30 minutes after histamine.

Intravenous Glucose Tolerance Test: (0.5 mg./Kg. as 20 per cent solution intravenously over 30")

F.B.S.	57
30"	181
60"	109
90"	100
150"	60

Oral Glucose Tolerance Test: 100 Gm.—orally

F.B.S.	70
30"	60
60"	75
90"	120
150"	80
210"	74

Course in Hospital: The patient was admitted to the Medical Service, where the diagnostic work-up was carried out and extensive supportive treatment given. A barium enema revealed the cecum and the ascending colon to lie on the left side of the abdomen just to the right of the descending colon (Fig. 1). No connection between the stomach and the colon was visible. The first gastro-intestinal series demonstrated a patent gastro-enterostomy, the pattern of the small bowel suggesting ileum rather than jejunum. There was a rapid filling of the colon, which suggested the possibility of a gastrojejuno-colic fistula. Re-examination, however, revealed that the anastomosis was between the stomach and the distal third of the ileum, without a connection with the large bowel. The terminal ileum was dilated moderately and exhibited both peristaltic and antiperistaltic waves (Fig. 2). Within two hours after the ingestion of barium, it was observed in the cecum.

A high-caloric, high-protein diet was tried, but no gain in weight or strength resulted. The patient was tried on a 4,500-calory diet containing 200 grams of protein, 110 grams fat, and 678 grams of carbohydrate. This she could not tolerate and an exacerbation of the diarrhea occurred. She continued to lose weight until she weighed only 90 pounds. Multiple blood transfusions and intravenous plasma and protein hydrolysates were given with some improvement in blood protein (total protein 4.5 with albumin 2.1 and globulin 2.4) and body weight (97 pounds).

It was felt that the patient would require jejunostomy feeding before she could be built up enough to stand a major operation. Therefore, under local anesthesia, on December 27, 1947, a Witzel type of jejunostomy was performed. There was relative freedom from adhesions and it became obvious at this time that there was a developmental anomaly of the gastro-intestinal tract with faulty rotation of the midgut. After some exploring, the duodenum was traced distally and a jejunostomy was performed at a point approximately 15 inches from the duodenojejunal junction. The abdominal opening was made in the left middle quadrant in an effort to have it out of the way of the gastric surgery to be performed subsequently.

The patient stood this procedure well and was started the same day on a special formula† of predigested food, 30 cc. per hour. This formula consists of amino acids, dextromaltose, cream, salt mixture, vitamins and water in such a proportion that 1 cc. contains about 1 calory. These feedings were tolerated quite well and were increased

† The formula used was essentially the same as described by Hollander, Rosenak and Colp.[9]

FIG. 1 FIG. 2A

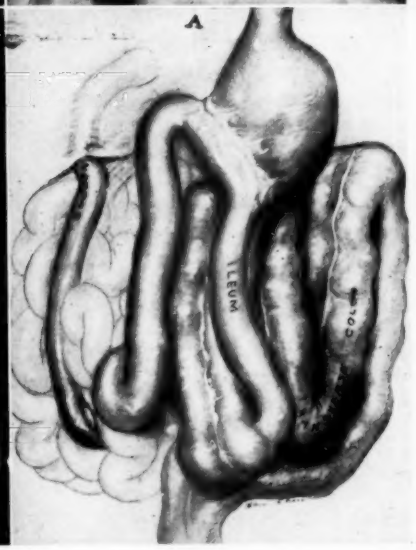

FIG. 2B FIG. 3

FIG. 1.—This barium enema revealed practically the entire large bowel to be situated in the left half of the abdominal cavity. There was no reflux of barium into the stomach, indicating that a gastrocolic fistula probably did not exist.

FIG. 2.—A gastro-intestinal series demonstrated the flow of barium into the colon within two hours. The small-bowel pattern suggests ileum. The limb of ileum labeled "A" represents the proximal limb, which is considerably dilated and in which both peristaltic and reverse peristaltic waves were seen on fluoroscopy. The distal limb "B" is also moderately dilated.

FIG. 3.—This drawing illustrates the congenital malrotation of the mid-gut and the gastro-ileostomy as found at operation. Note that the duodenum does not cross over the abdomen beneath the superior mesenteric vessels but continues downward in the right side into the jejunum, most of the jejunum being located in the right lower quadrant. Most of the large bowel is located in the left half of the abdomen. The gastro-ileostomy had been constructed at a point about 14 inches from the ileocecal valve. Both the afferent and the efferent limbs of ileum are considerably dilated.

soon to 150 cc. per hour. The patient complained of frequent abdominal cramps and had occasional nausea and vomiting but not enough to necessitate discontinuance. Occasional exacerbation of the diarrhea also occurred. In general, she progressed quite satisfactorily and on January 20, 1948, her total proteins were 6.9 Gm. with 5.5 Gm. alubumin and 1.4 Gm. globulin. She had gained in weight to 104 pounds. Her improvement continued, and before further surgery was carried out, her weight was 111 pounds, total protein 6.6 and A. G. ratio of 2:1.

She was up in a chair four days after the jejunostomy but she could not walk because of muscular weakness. She walked unassisted about three weeks after the jejunostomy, for the first time in seven months.

On February 12, 1948, under cyclopropane anesthesia, exploration was carried out. The anomaly of rotation was confirmed. The gastro-ileostomy was resected, removing the distal inch of remaining stomach and the attached ileum. An end-to-end aseptic anastomosis was made between the two ends of ileum using a single row of Halsted sutures of No. 60 cotton. A gastrojejunostomy was then formed, anastomosing the jejunum at a point about eight inches proximal to the feeding jejunostomy to the distal end of the remaining stomach.

Gross and microscopic examination of the resected specimen showed evidence of mild chronic inflammation of the stomach and the ileum in the region of the anastomosis. There was no area of erosion or ulceration.

Her postoperative course was uneventful. Jejunostomy feedings were continued for 12 days after the operation and then discontinued since her oral intake had become adequate. On February 29, 1948, she was discharged from the hospital weighing 117 pounds, having normal bowel movements and feeling very well.

She was seen about two months after her discharge, on April 21, 1948, at which time her serum proteins were normal and her weight had increased to 141 pounds. There was still slight ankle edema, thought to be related to old thrombophlebitis of deep thigh and pelvic veins. There had been occasional loose bowel movements on some mornings. The drainage from the old jejunostomy had practically ceased. When last seen, 10 months after operation, she was completely asymptomatic and the jejunostomy had closed.

DIAGNOSIS

Diagnosis should not be too difficult in most cases. The signs and symptoms in this case are typical. There was onset of diarrhea three days after the construction of the gastro-ileostomy, which might well have aroused suspicion of the error that had been made. The persistence of this diarrhea with marked loss of weight and strength would support such a suspicion. The absence of abdominal pain other than some crampy pain after defecating is somewhat unusual. Vomiting was not a prominent feature although it was occasionally present.

Brown and others summarized the signs and symptoms of the cases reported prior to 1947 and found that 17 of 24 complained of abdominal pain, 14 of 24 had diarrhea and 13 of 24 had some vomiting. Of 20 patients with statements regarding weight loss, 19 had lost weight. Fecal vomiting and hemorrhage had occurred in a few patients and six had developed ulcers in the ileum at the site of anastomosis. The signs and symptoms have also been discussed by Bailey and Castleton,[8] who summarized in table form all previously reported cases.

The rapid filling of the colon after swallowing barium was practically

diagnostic in this case. The lack of reflux into the stomach of barium given as a barium enema was evidence against a gastrocolic fistula.

Brown and others pointed out that serial barium-meal films of the gastrointestinal tract frequently show some refilling of the stomach after it had emptied. This was demonstrated from three and one-half to five and one-half hours after the barium meal by the reappearance of barium in the stomach from the ileum. This finding depends upon the flow of barium through the pylorus into the small bowel and on through the small bowel until it re-enters the stomach through the gastro-ileostomy. Therefore, it could apply only to those cases in which there had been a gastro-ileostomy performed without gastric resection. It also could not apply to those cases in which the pyloric obstruction is complete.

Bargen and Rankin[10] in 1930 cited 12 patients who had developed severe postoperative diarrhea due to ulcerative colitis. These symptoms began from 3 to 15 days after abdominal surgery, chiefly on the stomach or biliary system. This condition can usually be differentiated from a gastro-ileostomy by barium enema.

Gastro-ileostomy alone is less serious than when accompanied by a gastric resection. With gastrectomy, the duodenum, the jejunum and the proximal ileum are completely by-passed and the only appreciable food absorption is from the stomach and the terminal ileum. Without gastric resection, a part, depending on the degree of pyloric obstruction and the patency of the gastro-ileostomy stoma, of the food goes through the entire small bowel. Therefore, relatively few symptoms result from gastro-ileostomy when the major part of the food goes through the pylorus, as in several reported cases of many years' duration (one case of 23 years' duration reported by Smith and Rivers). Other cases with practically complete pyloric obstruction have the same rapid downhill course as those patients with gastric resection, such as one case reported by Smith and Rivers of three months' duration and a weight loss of 60 pounds.

The development of ileitis or ulceration of the ileum has been discussed by Rivers and Wilbur[4] and by Kogut and Stein.[5] This case had no ulceration and showed only mild chronic inflammation of the stomach and the ileum near the anastomosis.

PREVENTION

Most cases of gastro-ileostomy are probably associated with inexperienced surgeons. A few such errors may have resulted from the surgeon's failure to realize the importance of using the jejunum instead of the ileum for a gastro-enterostomy. Most, however, are probably the result of difficulty in differentiating between a loop of jejunum and a loop of ileum. The appearance of a single loop of small intestine may not be sufficiently characteristic of either jejunum or ileum to permit positive identification. Much more certain is the practice of identifying a loop of small bowel not by its appearance alone but by its relationship to known landmarks. The most useful landmark in choosing a loop of jejunum for gastro-enterostomy is the ligament of Treitz.

In the absence of the ligament of Treitz, as in the case reported here, an anomaly of rotation should be suspected and a loop should be selected by tracing the duodenum distally or by tracing the small bowel proximally from the cecum. The presence of many adhesions complicates the problem.

Although a loop of bowel picked up in the left upper quadrant beneath the transverse mesocolon will usually be jejunum, it must be identified with certainty before it is used in a gastro-enterostomy.

Dott[11] has beautifully described the embryologic changes in the intestinal tract and has pointed out many of the more frequent errors in rotation. McIntosh and Donovan[12] have discussed the clinical significance of faulty rotation and have given case histories illustrating these features.

The faulty development in this case is illustrated in Figure 3. This anomaly represents a derangement of the second stage of rotation, consisting of nonrotation of the midgut loop. This form of derangement is not uncommon and has been described by Dott.[11] Incomplete rotation of the midgut prevented the duodenum from becoming posterior to the superior mesenteric vessels; instead the duodenum coursed downward in the right side of the abdomen to the duodeno-jejunal junction and most of the jejunum remained in the right lower quadrant. Most of the small bowel on the left side of the abdomen was ileum ending in the ileocecal valve situated low in the midline. The cecum and ascending colon had not rotated in front of the superior mesenteric vessels but had come to rest chiefly to the left of the midline.

McIntosh and Donovan[12] reported one case with an anomaly practically identical with that present in this patient. Dott explained this anomaly as a result of the umbilical orifice being so large that it exerts no restraining influence on the return of the cecum through this orifice. This enlarged umbilical orifice allows the cecum to return to the abdominal cavity along with or before part of the small bowel, thus eliminating the factor which normally causes a rotation of the midgut.

In this case the malrotation caused the loops of ileum to be located in the left upper quadrant and the extensive adhesions prevented thorough exploration, thus accounting for the surgical error.

PREOPERATIVE TREATMENT

Many of these patients have lost much weight. Brown and others[7] stated that of the 20 cases reported in which there was a statement regarding weight loss, 19 had lost weight. Many are in poor nutritional state and a few are in a critical condition. Increased food intake with high protein and carbohydrate content is routinely given to these patients. Enriched formula feedings have been used and massive vitamin intake has been assured. However, food taken by mouth is very poorly assimilated and these measures seldom materially improve the patient's condition when the proximal bowel is excluded, as in gastro-ileostomies with partial gastrectomy. A good guide to the progress being made is afforded by following the patient's weight and serum proteins.

In seriously ill and markedly emaciated patients, intravenous feedings are necessary. Infusions of whole blood, plasma and amino acids may be of marked benefit. In this patient all these measures were tried but no material improvement could be obtained. Such a case provides an ideal indication for a feeding jejunostomy. Figure 4 illustrates the relationship of the jejunum, the ileum and the stomach after jejunostomy in this patient. A synthetic aliment similar to that described by Hollander, Rosenak and Colp[9] was used, beginning a few hours after jejunostomy, with marked success. The patient's weight and serum protein increased rapidly with reversal to normal of the A/G

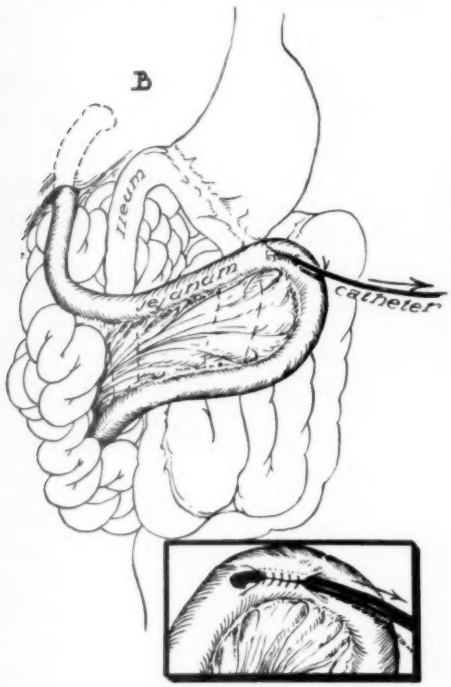

FIG. 4

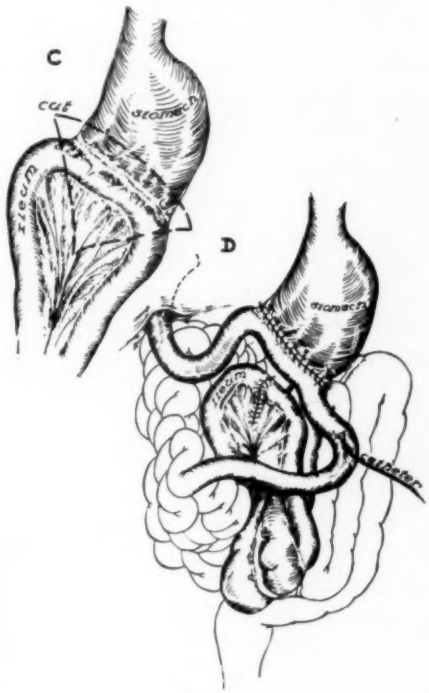

FIG. 5

FIG. 4.—A Witzel jejunostomy was performed at a point about 15 inches from the duodenojejunal junction. The abdominal opening was made well on the left side of the abdomen so that it would not interfere with the contemplated reconstructive surgery.

FIG. 5.—In the upper figure the broken lines indicate the limits of resection. After excising this area, an end-to-end anastomosis was made between the two ends of ileum. A gastrojejunostomy was completed to the jejunum at a point about 8 inches proximal to the jejunostomy; the lower figure shows the relationship between the gastrojejunostomy, the jejunostomy and the ileum when completed.

ratio. Within three weeks she was able to walk unassisted for the first time in seven months. It is very dubious that this patient could have survived the major operation of reconstructing a gastrojejunostomy without first having the benefit of a feeding jejunostomy.

In none of the previously reported patients has a feeding jejunostomy been done as a preliminary to the major reconstruction. In one case reported by

Smith and Rivers a temporary jejunostomy was done at the time of the reconstruction. Most of the previous reports stressed the importance of preoperative treatment, but very seldom was any estimate given as to how successful the preoperative measures had been. There were no observations on weight gain prior to operation and few observations on change in serum protein prior to operation.

A wise procedure would be to employ a feeding jejunostomy in those patients who are in poor nutritional status and who do not respond satisfactorily to forced feedings intravenously or by mouth.

OPERATIVE TREATMENT AND RESULTS

The desired treatment depends upon the existing circumstances. If a subtotal gastrectomy has already been done, the problem is different from that when only a gastro-ileostomy has been carried out.

Gastro-ileostomies without gastrectomy will be considered first. Twenty-two of the reported cases are in this category and all these patients were suffering from peptic ulcer, the gastro-ileostomy being done to help this condition. The following chart summarizes the treatment carried out in this group:

Operative Treatment in 22 Cases of Gastro-Ileostomy for Peptic Ulcer (Without Coincident Gastrectomy)

	Number of Cases	Results		
		Good	Poor	Unknown
1. Reconstruction of normal continuity	13	11	1*	1
2. Partial gastrectomy with gastrojejunostomy	4	4		
3. Reconstruction with pyloroplasty	2	1	1**	
4. Reconstruction with pyloroplasty and temporary feeding jejunostomy	1	1		
5. Reconstruction with posterior gastrojejunostomy	1	1		
6. Not stated	1	1		

* Ulcer recurred—satisfactorily treated by posterior gastro-enterostomy later.
** Ulcer pain recurred.

No deaths occurred in this group. Recurrence of duodenal ulcer occurred in two cases, one after simple reconstruction, the other after reconstruction with pyloroplasty.

There are really two main problems in the surgical treatment of gastro-ileostomy. First, the gastro-ileostomy must be corrected; second, the patient may still have the original difficulty to be treated, namely, the duodenal ulcer.

Ideally, the preferred surgical treatment would care for both these problems at one time. Depending upon one's views on the value of vagotomy, one may choose to take down the gastro-ileostomy, close the openings in the stomach and ileum and to perform a vagotomy with a pyloroplasty or gastrojejunostomy if pyloric obstruction exists. Instead, one may prefer to carry out a subtotal gastric resection with gastrojejunostomy, after taking down the

gastro-ileostomy. Either of these two procedures can be carried out if the patient is a good surgical risk. If not a good risk, it still may be possible in some to take down the gastro-ileostomy and resect the vagus nerves. Usually some effort to treat the ulcer should be made at the same time the gastro-ileostomy is corrected. Otherwise there is a good possibility that the duodenal ulcer will give further difficulty. If there is marked pyloric obstruction, some means of exit for the gastric contents must be provided. It is to be noted that four cases had a subtotal gastric resection carried out with good results in each case.

The operative treatment for those cases of gastro-ileostomy in which a partial gastrectomy already has been done requires only the correction of the gastro-ileostomy, since the ulcer probably requires no further treatment. Of the three cases with gastric resection complicated by gastro-ileostomy, two were for ulcer and one was for carcinoma of the stomach. The patient with carcinoma died 36 hours after the original operation, the gastro-ileostomy being found at autopsy. The other two cases were treated by taking down the gastro-ileostomy and constructing a gastrojejunostomy. The follow-up of these two cases revealed no further difficulties.

One satisfactory procedure is to resect the area of anastomosis including the distal inch or so of the stomach and the ileum involved in the anastomosis between clamps. An end-to-end anastomosis is then carried out between the two ends of the ileum and a Polya gastrojejunostomy is performed. This block type of resection was done in this case and it is felt that this offers some advantages over disconnecting the anastomoses, closing the ileal stoma and using the original gastric stoma in the gastrojejunostomy. The block resection can be done more quickly and possibly with less soiling. More confidence is placed in an anastomosis between freshly cut edges than between old and fibrotic edges. It is believed that there is less danger of complications such as leakage at the anastomosis or obstruction. This procedure is illustrated in Figure 5.

One cannot assume because of the uniformly good results in the reported cases that the reconstruction of a gastro-ileostomy is not a serious undertaking. Many patients are probably reoperated upon by the same surgeon who made the original error and these are not reported. It is also probable that many patients unsuccessfully operated upon for this condition are not reported. If the unreported cases were reviewed, it is extremely likely that the statistical results would be considerably different.

SUMMARY

A case is presented of a gastro-ileostomy following subtotal gastric resection for duodenal ulcer. In the treatment of this patient, a feeding jejunostomy was first established which greatly improved the general condition of the patient. Several weeks later there was a successful resection of the gastro-ileostomy and reconstruction of a gastrojejunostomy with end-to-end anastomosis between the two ends of ileum.

There was an associated anomaly of rotation of the midgut which predisposed the patient to this surgical error. Absolute identification of the anatomy before performing a gastro-enterostomy is necessary.

Vigorous preoperative treatment is essential to restore these patients to good condition. A preliminary jejunostomy for feeding is of value in the severely emaciated patient who fails to respond to other measures.

A block resection of the gastro-ileostomy is advocated for those patients who have had subtotal or partial gastric resection. For those who have not had a gastric resection, satisfactory results may be obtained by taking down the gastro-ileostomy and combining this with a subtotal gastrectomy or a vagotomy.

Twenty-four instances of gastro-ileostomy have been reported previously in sufficient detail for study. Twenty-two of these were of gastro-ileostomy done without gastric resection. Only two, plus a third reported here, were gastro-ileostomies following a partial gastric resection.

It is probable that the reported instances of this type of surgical error represent only a small percentage of the actual number of such errors. The uniformly good results in the reported cases probably are not indicative of the results in the group not reported.

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Editorial . . .

The Inquiring Mind

All surgeons aware of their responsibility to their profession and to society must inevitably be concerned with the training of those who will succeed them. There are often two components of training. One is the imparting of technical skills or knowledge. The second consists of imparting a point of view, or philosophy, to the trainee. In the trades, the union or the employer may be equally desirous of imparting to the trainee a particular philosophy, yet it is obvious that a man can be skilled at a trade no matter what his philosophy. In other fields, the point of view is an integral part of the training, just as important as the technical skill. Thus the training of a soldier involves not only the imparting of technical skill but of imbuing the individual with an unwavering loyalty towards his country. Without this second component the technical skills are useless, or may even be harmful to the accomplishment of the desired goal: a well-trained and loyal soldier. The training of a surgeon requires the imparting of both technical knowledge and a philosophy. The latter is the more important of the two.

A knowledge of the desired objective is implicit in any training program. That part of a surgeon's life in which he fulfills the objectives of his training rarely lasts more than 30 years. Part of the training objective might be considered as teaching the technical skills which will be required by the surgeon during these 30 active years; but it is impossible to predict the surgical procedures which he will be called upon to perform. His technical training, therefore, must be largely concerned with basic skills and knowledge, rather than with particular technics which may well become obsolete. For example, mastoidectomies, and thoracotomies for empyema following pneumonia, are rarely performed now, owing to the discovery of chemical and organic materials which are effective in the control of infections. The surgeon of tomorrow may be operating in different fields. The emphasis may pass from the surgical treatment of infections to that of the correction of congenital abnormalities. The field of vascular surgery is rapidly enlarging its scope. The surgeon may soon be operating under direct vision within the heart itself. Future developments of medical science may eliminate much of the surgical treatment of conditions resulting from degenerative processes. At present the radical local extirpation of cancer by surgical means constitutes the best weapon against this condition. Enormous resources are now being made available for investigation of the cause and cure of cancer. When such research reaches fruition surgical treatment of the disease may become obsolete.

It is apparent, therefore, that the modern training of a surgeon must include the acquisition of a broad background in fundamental fields of

medical knowledge. Physiology, biochemistry, anesthesia and probably radiation and nuclear physics, all will provide a background which will help the surgeon of tomorrow to cope with the inevitable advances in medical science in the coming years. The examining boards in the surgical specialties should recognize the importance of these fields of knowledge, instead of laying major emphasis on the preclinical fields of anatomy and pathology. Certainly it is just as important for the surgeon to be thoroughly acquainted with the important subjects of nutrition, fluid and electrolyte balance and the dynamics of cardiorespiratory physiology, as it is for him to know the anatomy of the region in which he is operating and the pathologic conditions which he may encounter. A knowledge of anatomy and pathology is just as essential as it was 50 years ago, but to halt there in the training of the modern surgeon is to overlook the advances of the past generation.

Of far greater importance than teaching either a fundamental background or a technical skill is the indoctrination of the surgical aspirant with a philosophy. This philosophy is that of the inquiring mind. The ability to pose pertinent questions involves intelligence and implies the ability to draw logical conclusions from the answers. It is diametrically opposite to the type of mind which unquestioningly accepts the written or spoken word of considered authorities. This unquestioning attitude has no place in the field of science. It was responsible for the long stagnation in scientific thought through the dark ages, which in the field of anatomy perpetuated the errors of the Galenic school for centuries, until Vesalius questioned these dogmas and threw new light upon anatomy and related subjects by direct observation.

None will venture to disagree that the inquiring mind is essential to scientific progress. That it is also a valuable and essential attribute of the modern practicing surgeon is less generally realized. The practice of medicine is not the simple acquisition of a set of rules which when applied to the problem posed by the particular patient will always result in the correct diagnosis or correct therapy. The patient with an ulcer of his duodenum or stomach does not always present the classical symptoms of epigastric pain between meals, relieved by the taking of food or alkali. The practicing physician or surgeon who relies upon a text-book set of rules to make a diagnosis of appendicitis will find himself frequently in error. Questioning is an integral part of the elucidation of symptoms. The correct diagnosis of disease depends upon a careful evaluation of all the available evidence. The same exercise of judgment is required in therapy as in diagnosis. Dependence upon simple rules of thumb never characterized the competent physician or surgeon.

The inquiring mind is typical of youth. It is exemplified by what are sometimes regarded as the "tiresome" questions of small children. It characterizes the attitude of intelligent students through school, college and postgraduate studies. Too often, through incompetent pedagogy, this attitude of mind is gradually stifled, with the result that a graduating student leaves the halls of learning with a set of ideas and concepts which gradually harden into an unyielding structure.

THE INQUIRING MIND

It may be doubted that it is possible to cultivate the inquiring mind in one field of knowledge without disturbing the fixed ideas and conceptions which have already been formed in other fields. Yet all of us have known outstanding leaders in the surgical profession who eagerly embrace new developments in surgery, but who may be completely lacking in this attitude of mind when it comes to politics, literature, art, etc. The inquiring mind is one which is actively engaged in the search for truth and knowledge. It is impossible for one individual to master all knowledge and it is easier to accept authority in other fields than to question it.

It is possible for the student to acquire this attitude of mind at an early stage in his professional training and to retain it throughout his active career, because with good pedagogy the questioning attitude will become an integral part of the learning process. A properly trained student will not accept unwarranted conclusions which may appear in published medical articles, but will study the text and draw his own conclusions. The poorly trained student of medicine, on the other hand, is likely to accept conclusions of this character because of the authority of the written word. It is obvious which of these men will be the better practitioner.

Why is this invaluable component of training occasionally neglected? First, the teacher of surgery may be unaware of the importance of this aspect of training; and secondly, he may discourage questions because of the unconscious fear that if he does not know the answer he will "lose face" in the eyes of his students. The importance of inculcating this attitude of mind in young surgeons will become apparent if the matter is given thoughtful consideration. The unconscious fear of betraying ignorance can be overcome if boldly stated and honestly faced.

A great deal has been written in the past generation about the training of surgeons. Much of it is concerned with where he is to be trained, and how long, and the qualifications of his instructors. Much attention has been paid to evaluating his training by examination. Too little thought has been devoted to the objectives of training. Let us be sure of our surgical goals. Because of our concern with the formal indoctrination of skills, we should not neglect an essential philosophy. The best surgeons of tomorrow, as of yesterday, will always be those with inquiring minds.

JOHN H. GIBBON, JR.

LETTER TO THE EDITOR

DEAR SIR:

After reviewing this most interesting paper of Dr. Clarence C. Eckert, I should like to call attention to the fact that, in my opinion, it is most difficult indeed, in our present state of ignorance regarding carcinoma, to place certain cases of carcinoma of the breast in the category of "inoperable"; and I must confess that I am not in agreement with Haagensen and Stout's classification, on which Doctor Eckert's paper is based.

In 1929, in collaboration with Dr. Dean Lewis, I published a follow-up study of almost 1,000 cases of carcinoma of the breast which had been operated upon by Doctor Halsted and Doctor Finney, Sr., together with all of their residents from 1889 to 1929, inclusive. This follow-up revealed many points of interest. The operation performed by the various operators—all Halsted-trained men—was a typical Halsted radical mastectomy, so that the operative procedure was constant. Pathologic diagnoses also were made by Dr. W. H. Welch and his staff in the Department of Pathology, of the Johns Hopkins Hospital, so that there was no variation in the interpretation of the specimens and microscopic sections.

With this background, it was soon discovered in the follow-up that dogmatic statements in regard to prognosis following radical mastectomy for carcinoma of the breast should *not* be made, and certainly the so-called classification of inoperability by Haagensen and Stout did not hold for this series of almost 1,000 cases. The statement by the latter authors to the effect that when carcinoma of the breast develops during pregnancy or lactation it is always inoperable, is literally untrue. There were patients operated upon, not only in the Johns Hopkins Hospital but at other hospitals in Baltimore, for carcinoma of the breast during pregnancy who lived for a period of years or are still living. One patient with whom I was personally connected has lived about ten years. This patient had a very malignant medullary type of carcinoma of the breast with metastasis to the axillary glands that developed midway in pregnancy. After a radical mastectomy had been performed, the ovaries and uterus containing the fetus were removed and this patient is alive and well today. There are others in this series who survived for some years and who were lost track of, but they may well be alive.

The second point, namely, that edema of the skin or nodular implantation of the growth near by the original tumor is a sign of inoperability is likewise inaccurate. There were a number of patients in this series at the Johns Hopkins Hospital in whom edema of the skin had occurred, and also subcutaneous implantation of the tumor, who were operated upon successfully and had survived for a number of years at the time of the follow-up study. One patient in particular, operated upon by Dr. William Sowers while he was resident surgeon at the Johns Hopkins Hospital in 1905, a woman, was still alive 25 years after, at the age of 80 plus. This patient survived a radical mastectomy for an ulcer-

ated carcinoma of the breast that had not only ulcerated through the skin over the entire dome of the breast, resulting in a foul-smelling wound with implantations in the skin surrounding the ulceration, but also had metastasis to the axillary and supraclavicular lymph nodes. Doctor Sowers performed a very radical operation upon her, removing the breast and the underlying structures to the chest wall, dissecting the axillary nodes and at the same time going above the clavicle, as was done in those days, and removing the lower cervical chain of lymph nodes, which were invaded. The operation consumed more than five hours, but the patient was cured and, as I stated above, was alive 25 years later at the age of 80 plus.

It is, of course, to be admitted that this was one case in practically one thousand, but when one is dealing with a human being and with a relatively unknown condition such as carcinoma, it seems to me that no stone should be left unturned to save the patient's life. I think few will deny that, had not Doctor Sowers performed such a radical and meticulous operation, the patient would not have survived as long as she did.

In any series of breast tumors there are patients with ulceration of the skin who have lived a number of years following radical mastectomy and have been much better off following such an operation than they would have been had the ulceration been treated palliatively, with the consequent infection and foul discharge, to say nothing of the bleeding which often occurs in those patients on whom an operation has not been performed.

I think anyone adhering to Haagensen and Stout's classification would be led astray and that a number of patients who should have radical mastectomies would probably be denied their one chance to be cured.

The five-year cures that have often been discussed is essentially misleading. The word survival should be substituted for cure. In the series studied by us at the Johns Hopkins Hospital there were recurrences in every decade, up to 33 years postoperatively in two cases.

It would seem to me that the aim of the surgeon in treating carcinoma of the breast should be not only to attempt to cure the patients of the disease process but also to prolong their lives and make them physically and mentally as comfortable as possible. If it were possible completely and minutely to examine the entire bodies of persons apparently cured of carcinoma, it might well be demonstrated that we in some manner retarded the spread of the disease by removing the original tumor and that people may die with, if not of, the residual depositions of malignant growths. The report of Peugniez, who did a partial gastrectomy for carcinoma of the stomach at the Hotel Dieu in Paris, and who, 25 years later, when the patient returned to the hospital and died of lobar pneumonia, found at autopsy some adenocarcinoma in the retroperitoneal glands which were histologically indistinguishable from the primary carcinoma is a famous case. Thus, the growth had lain latent over that period of time. It would seem, therefore, that it behooves the surgeon to perform within reason, thorough extirpation of carcinomatous growths whenever the region involved and the extent permit such procedure.

Local recurrence in the skin, in several instances in my own personal experience, have been successfully treated by radical secondary excision. In the absence of distant metastases or local signs of inoperability, such as fixation due to involvement of the chest wall, brachial plexus or the great vessels, it is our belief that the great majority of patients with carcinoma of the breast should be given the opportunity of having radical mastectomies.

Another point which is not emphasized in Doctor Eckert's paper, or that of Haagensen and Stout in their classification of "categorically inoperable cases," is the prognosis depending on the histologic type of tumor. Almost everyone who has treated carcinoma of the breast knows, or should know, for instance, that a duct cell or comedocarcinoma of the breast, no matter how extensive the ulceration or edema, offers far the best prognosis of all the malignant tumors of the breast. It would, of course, be possible to have such a tumor of the breast in a late stage and still, in spite of the external appearance of inoperability, be amenable to radical surgical extirpation. These opinions are based upon many years' experience of the staff of the Johns Hopkins Hospital associated with the late Doctors Halsted, Finney, Bloodgood, Heuer, McClure, Reid, Holman and many of the resident surgeons connected with Doctor Halsted's staff who were intensely interested in the study of malignant tumors of the breast. I think that in our present state of knowledge all malignant tumors of the breast should be treated surgically and by a radical operation similar to the one proposed many years ago by Doctor Halsted and unimproved since. It transcends human knowledge, at present at least, to prognosticate accurately in such cases unless as stated before, there are distant metastases or local involvement of structures which are obvious and need no discussion. The efficacy of any other form of therapy, including deep roentgen, before or afterwards, has never been convincing to me and certainly, in my opinion, radical surgical excision is still the therapeutic method of choice.

The main difficulty with the classification "categorically inoperable" is that it is too categorical.

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BOOK REVIEWS

REVIEW OF ACUTE INTESTINAL OBSTRUCTION by Rodney Smith, Asst. Surgeon, St. George's Hospital, London. The Williams & Wilkins Co., Baltimore, Md., 1948. Price $5.00; 240 pages.

This book presents the mechanisms of acute intestinal obstruction due to various causes and discusses the pathological physiology and its treatment. The last one hundred pages are concerned with the individual varieties of acute intestinal obstruction, and because of the large number can be only briefly discussed.

Emphasis is given to conservative decompression with indications for operation, with the author's opinion being that aseptic types of anastomoses are to be preferred. While there is more or less complete agreement that there are types of acute intestinal obstruction which can be relieved temporarily or permanently with the use of the Miller Abbott tube alone, not all will agree with the statement that "once the balloon of the Miller Abbott tube is in the duodenum, decompression can always be achieved." While for the most part the local intraperitoneal instillation of sulfonamides has been abandoned in this country, the author believes strongly that it should be used and devotes a chapter of discussion in support. There is a paucity of discussion in regard to electrolyte control and replacement, and the author cites his lack of experience with parenteral protein alimentation due to lack of supplies in England.

While nothing new is presented, the book is an excellent review of the subject, recognizing the limitations of space.

DAVID V. HABIF, M.D.

PREOPERATIVE AND POSTOPERATIVE CARE OF SURGICAL PATIENTS by Hugh C. Ilgenfritz, St. Louis, C. V. Mosby Company, 1948, price $10.00.

This book contains much useful information and on the whole fairly represents the principles and methods accepted by present-day surgery. The author provides a useful set of rules and procedures for actual preoperative and postoperative situations. He has chapters devoted to the problems of biliary, gastric, colonic and thoracic surgery, as well as to general subjects such as wound care, surgical infections and shock.

The book suffers somewhat from the author's efforts to cover too broad a range of topics. His discussions of physiological chemistry and of the techniques of laboratory determinations are too abbreviated and elementary to be worthwhile. The author writes in a didactic manner, and a more imaginative discussion of conflicting viewpoints of the controversial problems would have been desirable and, very likely, useful.

NICHOLAS S. GIMBEL, M.D.

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KOSMAK, GEO. W. RUTHERFORD, ROBERT N. *Editors*	*Transactions of The Third American Congress on Obstetrics and Gynecology.* Western Journal of Surgery Publishing Co., Portland, Oregon, 1948.

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ANNOUNCEMENT

THE KAPPA DELTA AWARD FOR RESEARCH IN ORTHOPEDIC SURGERY

The National Council of the Kappa Delta Sorority has inaugurated a prize of one thousand dollars to be given annually by the American Academy of Orthopaedic Surgeons for the best research in orthopedic surgery performed during the year by an individual in the United States. The first award, for the year 1949, will be announced at the seventeenth annual convention of the Academy in New York, February 11, 1950. Those wishing to compete for this prize can secure further information from Dr. Walter Stuck, 1426 Nix Professional Building, San Antonio, Texas, Chairman of the Award Committee for 1949.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY.

John H. Gibbon, Jr., M.D.

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